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XUM

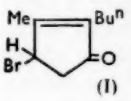
541. *The Relative Stabilising Influences of Substituents on Free Alkyl Radicals. Part V.*[1] *Selective Bromination by N-Bromosuccinimide.*

By R. L. Huang and (Miss) Pearl Williams.

It has been established that in bromination by *N*-bromosuccinimide, a phenyl group has a greater stabilising effect than a benzoyl or a carboxyl group on the intermediate free radical.

Wohl–Ziegler bromination of unsaturated substances is highly specific, occurring invariably on the carbon atoms adjacent to the unsaturated centres. This follows from the mechanism of the reaction,[2] in which the radical intermediate involved is stabilised by resonance by the unsaturated group. In a substance $X{\cdot}CH_2{\cdot}CH_2{\cdot}Y$, therefore, in which both X and Y are unsaturated substituents, both methylene groups would be open to attack and, provided steric complications are absent, bromination would proceed by the route involving the radical intermediate of greater stability. Selective bromination therefore provides a means by which such stabilising effects can be compared. To this end we have studied the bromination, under catalysis by light or benzoyl peroxide, of nine substances of the general structure $X{\cdot}CH_2{\cdot}[CH_2]_n{\cdot}CH_2{\cdot}Y$ ($n = 0$ or 2), in which X and Y are phenyl, acetyl, ethoxycarbonyl, carboxyl, or benzoyl.

Few of the many published results[3] are useful for our purpose. Buu-Hoï[4] reports that bromination of 6-methylhept-5-en-2-one gives the α-bromo-ketone but quotes no yields. For a decisive evaluation of the relative stabilising effects of the substituents a yield of 50% or higher of the bromo-compound is necessary; but on the assumption that the main product isolated indicates the main course of the reaction, it can be inferred that the carbonyl group stabilises the intermediate alkyl radical more than the olefinic double bond does. Gensler *et al.*,[5] in a synthesis of elaidic acid, brominated methyl undec-10-enoate and obtained a mixture of the 9- and the 11-bromo-ester, for which the intermediate would be the mesomeric radical, $CH_2{:}CH{\cdot}\dot{C}H{\cdot}[CH_2]_7{\cdot}CO_2Me$. However, since the total yield did not exceed 42%, no conclusion could be drawn regarding the stabilising influences of the olefinic double bond and the ester group. Dihydrocinerone, on bromination, gave the product (I);[6] here, although a direct comparison cannot be made of the carbonyl group and the olefinic double bond because they are in conjugation, the position of bromination is not surprising considering the presence in the radical intermediate involved of the extended conjugated system $O{=}C{-}C{=}C{-}C{\cdot}$ which is not found in the alternative radical ($C{=}C{-}CO{-}C{\cdot}$). This situation finds some analogy in the benzoyl and the phenyl group ($Ph > Ph{\cdot}CO$) (see below).



(I)

The present work involved selective bromination of (*a*) β-phenylpropionic acid, (*b*) its ethyl ester, (*c*) 4-phenylbutan-2-one, (*d*) 6-phenylhexan-2-one, (*e*) lævulic acid, (*f*) 6-oxoheptanoic acid, (*g*) 6-oxo-6-phenylhexanoic acid, (*h*) ethyl 6-oxo-6-phenylhexanoate, and (*i*) 4-benzoyl-1-phenylbutane. Of these, only (*a*) and (*i*) afforded unambiguous indications of the relative stabilising influences of the substituents compared, namely, $Ph > CO_2H$ or $Ph{\cdot}CO$. In the other cases the bromo-compound could not be isolated, or was obtained in less than 50% yields, while in (*e*) and (*f*) no product was isolated.

Bromination of β-phenylpropionic acid proceeded smoothly to give the β-bromo-acid

[1] Part IV, Huang and Singh, *J.*, 1958, 891.
[2] Bloomfield, *J.*, 1944, 114; Ford, *J.*, 1955, 2529.
[3] See Djerassi, *Chem. Rev.*, 1948, **43**, 271; Waugh, "*N*-Bromosuccinimide, Its Reactions and Uses," Arapahoe Chemicals, Inc., Boulder, Col., U.S.A., 1951.
[4] Buu-Hoï, *Experientia*, 1946, **2**, 310.
[5] Gensler, Behrman, and Thomas, *J. Amer. Chem. Soc.*, 1951, **73**, 1071.
[6] Soloway and LaForge, *ibid.*, 1947, **69**, 979.

in 58% yield (both the α- and the β-bromo-acids have previously been reported). The intermediate radical $Ph\cdot\dot{C}H\cdot CH_2\cdot CO_2H$ was clearly involved, so the phenyl group has more stabilising effect than a carboxyl group.

Bromination of ethyl β-phenylpropionate also took place readily, but the resulting bromo-ester could not be isolated. An attempt to convert it into the bromo-acid by treatment with an excess of acetic acid in the presence of hydrogen bromide gave cinnamic acid.

6-Oxo-6-phenylhexanoic acid gave a bromo-acid (48% yield) which is considered to be the 5-bromo-acid, on the following evidence. With boiling pyridine or dimethylaniline, or with potassium acetate in hot acetic acid it gave, not an unsaturated acid, but a hydroxy-acid (42—57%) which was oxidised by potassium permanganate to succinic and benzoic acid, both in yields of over 50%. Although the α-hydroxy-acid would afford these products, so would the δ-hydroxy-acid (by analogy with the permanganate oxidation of 3-hydroxytridecan-2-one to decanoic, and not undecanoic, acid [7]). Conversion of the bromo-acid by pyridine and dimethylaniline into a hydroxy-acid could be explained by the intermediate formation of a δ-lactone (formed by nucleophilic attack of the carboxylate ion) although this would not be possible with the α-hydroxy-acid. This, together with the observation that the hydroxy-acid reacted with periodic acid, favours the δ-bromo-acid structure for the bromination product.

The bromination product of ethyl 6-oxo-6-phenylhexanoate could not be isolated, and hydrolysis by a variety of reagents gave only small quantities of the hydroxy-acid obtained as above.

4-Benzoyl-1-phenylbutane reacted with *N*-bromosuccinimide readily on irradiation, giving high yields (66%) of the δ-bromo-ketone $Ph\cdot CO\cdot[CH_2]_3\cdot CHBrPh$, whose constitution was ascertained by hydrolysis with aqueous potassium hydroxide to the hydroxy-ketone $Ph\cdot CO\cdot[CH_2]_3\cdot CHPh\cdot OH$, which on Oppenauer oxidation afforded the known 1 : 5-diketone. That the bromo-derivative was not the alternative α-bromo-ketone was further substantiated by its failure to form an aminothiazole derivative with thiourea,[7] and by the inertness of the derived hydroxy-ketone towards periodic acid. The course of bromination is therefore without doubt, and indicates that the phenyl group has greater stabilising capacity than the benzoyl group.

Among the unsuccessful studies, lævulic acid decomposed *N*-bromosuccinimide in chloroform or benzene (the acid being insoluble in carbon tetrachloride) under a variety of conditions. 6-Oxoheptanoic acid behaved similarly, though to a smaller extent. 4-Phenylbutan-2-one gave a highly unstable product, while 6-phenylhexan-2-one afforded a liquid which on degradation by the established methods gave a mixture from which no information concerning the structure of the bromo-compound could be obtained.

Experimental

Unless otherwise stated, bromination was carried out in " AnalaR " carbon tetrachloride in an atmosphere of nitrogen, with illumination by a 100 w incandescent lamp. *N*-Bromosuccinimide was crystallised quickly from hot water, and thoroughly dried before use. Microanalyses were by Dr. W. Zimmermann of Melbourne.

β-Phenylpropionic Acid.[8]—This acid (3·1 g., 0·021 mole) and *N*-bromosuccinimide (2·86 g., 0·016 mole) gave the β-bromo-acid, m. p. 141—142° (2·1 g.). Fittig and Binder [9a] report m. p. 137° for the β-bromo-acid and Senter and Martin [9b] record m. p. 52° for the α-bromo-acid.

Ethyl β-Phenylpropionate.—The ester (n_D^{24} 1·4927; 6·23 g., 0·035 mole) and *N*-bromosuccinimide (4·9 g., 0·028 mole) were irradiated in carbon tetrachloride (25 c.c.) for 35 min. A pale yellow solution resulted. Succinimide (m. p. 126—127°; 2·7 g., 0·028 mole) was filtered off, and the filtrate concentrated under reduced pressure at <50°. The residue was kept in a mixture of glacial acetic acid (35 c.c.) and hydrobromic acid (*d* 1·7; 13 c.c.) at 28° for 5 days.

[7] Cf. Huang, *J.*, 1957, 2528.
[8] Huang, *J.*, 1957, 1342.
[9] (*a*) Fittig and Binder, *Annalen*, 1879, **195**, 132; (*b*) Senter and Martin, *J.*, 1917, 447.

After the second day the ethyl acetate produced was removed at 50—60° under partial vacuum. On addition of water and chilling cinnamic acid separated (3·8 g., 93% yield), having m. p. and mixed m. p. 131—134° after recrystallisation from chloroform–carbon tetrachloride (mixed with β-bromo-β-phenylpropionic acid it melted at 110—121°).

6-Oxo-6-phenylhexanoic Acid.—This acid [10] (m. p. 77—79°; 5·4 g., 0·026 mole) and *N*-bromosuccinimide (4·0 g., 0·022 mole) in carbon tetrachloride (50 c.c.), were irradiated for 1·75 hr., some bromine and hydrogen bromide being evolved. On cooling, the succinimide was filtered off (1·8 g., 0·018 mole). The filtrate was taken up in much ether, washed twice with water (to remove traces of succinimide), once with aqueous sodium hydrogen sulphite, and dried, and the solution was concentrated. On addition of light petroleum (b. p. 40—60°), *5-bromo-6-oxo-6-phenylhexanoic acid* separated (5·6 g., 89%), having m. p. 107—109° (2·95 g., 48%) after recrystallisation from benzene–*cyclo*hexane (Found: C, 50·8, 50·3; H, 4·6, 4·6; Br, 28·4. $C_{12}H_{13}O_3Br$ requires C, 50·55; H, 4·6; Br, 28·0%). Other bromination experiments included: (*a*) use of a higher molar proportion of the bromo-imide, which gave a somewhat lower yield; (*b*) illumination for 1 hr., which resulted in incomplete reaction; (*c*) catalysis by benzoyl peroxide (without irradiation) which caused deterioration of the yield and purity of the product; and (*d*) use of chloroform as solvent, which appeared to bring about much more decomposition of the reagent (evolution of hydrogen bromide and bromine).

The bromo-acid (0·3 g.) was boiled with pyridine (5 c.c.) for 21 hr., then poured on ice and hydrochloric acid, and the product isolated by ether-extraction, giving *5-hydroxy-6-oxo-6-phenylhexanoic acid*, m. p. 107—110° (0·1 g., 50%); it had m. p. 125—127° after recrystallisation from ethanol–benzene, from which it separated in needles (Found: C, 64·7; H, 6·4. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%). Alternatively, the bromo-acid (1 g.) was boiled with dimethylaniline (15 c.c.) for 40 min. in nitrogen, to give the same hydroxy-acid (0·4 g., 59% yield); and when the bromo-acid (2·8 g.) and potassium acetate (3·4 g.) were heated in acetic acid (20 c.c.) at 100° for 4 hr., then boiled gently for 0·5 hr., working up gave the above hydroxy-acid, m. p. and mixed m. p. 124—126° (47%) (Found: C, 65·2; H, 6·25%).

The hydroxy-acid (0·13 g.) in acetone (5 c.c.) was treated during 1·5 hr. with potassium permanganate (0·5 g.) and magnesium sulphate (0·06 g.) in water–acetone in 4 portions. After 0·5 hour's refluxing, 10% aqueous sodium carbonate (10 c.c.) was added, and the manganese dioxide filtered off. The filtrate was heated to remove acetone, then washed once with ether, acidified with 5N-sulphuric acid and extracted 4 times with light petroleum. The aqueous layer was then continuously extracted (24 hr.) with ether. Both extracts were dried and concentrated. Benzoic acid separated from the petroleum extract (m. p. and mixed m. p. 120—123°; 30 mg., 50%), and succinic acid (m. p. and mixed m. p. 183—185°; 33 mg., 53%) was obtained from the ethereal extract.

4-Benzoyl-1-phenylbutane.—Cinnamylideneacetophenone (m. p. 102—104°, prepared in 88% yield from acetophenone and cinnamaldehyde by the method described for benzylideneacetophenone [11]) was hydrogenated in ethyl acetate over Raney nickel to give 4-benzoyl-1-phenylbutane, m. p. 45—47° (87% yield) after recrystallisation from methanol (lit.,[12] m. p. 47°). This ketone (3·5 g., 0·015 mole) and *N*-bromosuccinimide (2·1 g., 0·012 mole) in carbon tetrachloride (15 c.c.) after illumination for 0·75 hr. and removal of succinimide (1·1 g., 0·011 mole), gave *4-benzoyl-1-bromo-1-phenylbutane*, needles (from *cyclo*hexane), m. p. 109—111° (2·2 g., 59%) raised to m. p. 112—114° (needles) on further recrystallisation from the same solvent (Found: C, 64·7; H, 5·3; Br, 25·4. $C_{17}H_{17}OBr$ requires C, 64·3; H, 5·4; Br, 25·2%). Irradiation for 2 hr. gave 66% of a product of m. p. 111—113°.

This bromo-ketone (0·95 g.) in dioxan (10 c.c.) was boiled with 5% aqueous potassium hydroxide (25 c.c.) for 1·5 hr. The organic product was taken up in ether, washed with much water, dried, and concentrated, to give *4-benzoyl-1-phenylbutan-1-ol*, m. p. 77—78° (0·4 g., 53%) raised to m. p. 79—80° after recrystallisation from *cyclo*hexane from which the alcohol separated as needles (Found: C, 79·8; H, 7·2. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). Treatment of the bromo-ketone with boiling pyridine or dimethylaniline in the usual way gave intractable oils.

The above hydroxy-ketone (1·25 g.) in *cyclo*hexanone (30 c.c.; freshly distilled) was refluxed with aluminium *iso*propoxide (3 g.) in toluene (150 c.c.) for 1·25 hr. The *cyclo*hexanone was

[10] Fieser and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1948, **70**, 3352.
[11] *Org. Synth.*, Coll. Vol. I, 1st edn., p. 71; cf. Scholtz, *Ber.*, 1895, **28**, 1730.
[12] Borsche and Wolleman, *Ber.*, 1912 **45**, 3721.

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steam-distilled, and the aqueous residue extracted with ether (*ca.* 200 c.c.), washed twice with 2N-sulphuric acid and once with water, dried, and concentrated, giving 1 : 3-dibenzoylpropane, m. p. 58—62° (1·1 g., 92%). Recrystallisation from methanol gave laminae, m. p. 67—68° (0·8 g., 67%) (Found: C, 80·45; H, 6·5. Calc. for $C_{17}H_{16}O_2$: C, 80·95; H, 6·35%). Japp and Michie [13] report m. p. 67·5°. The dioxime, recrystallised from methanol, melted at 162—163°. A faster rate of heating gave m. p. 156—158° (Found: C, 72·5; H, 6·4; N, 9·5. Calc. for $C_{17}H_{18}O_2N_2$: C, 72·35; H, 6·4; N, 9·9%). Milone and Venturillo [14] report m. p. 165—166°.

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[13] Japp and Michie, *J.*, 1901, **79**, 1023.
[14] Milone and Venturillo, *Gazzetta*, 1936, **66**, 808.

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542. *Triterpenoids. Part LV.*[1] *The Stereochemistry of Alcohols Derived from Glutinone (Alnusenone).*

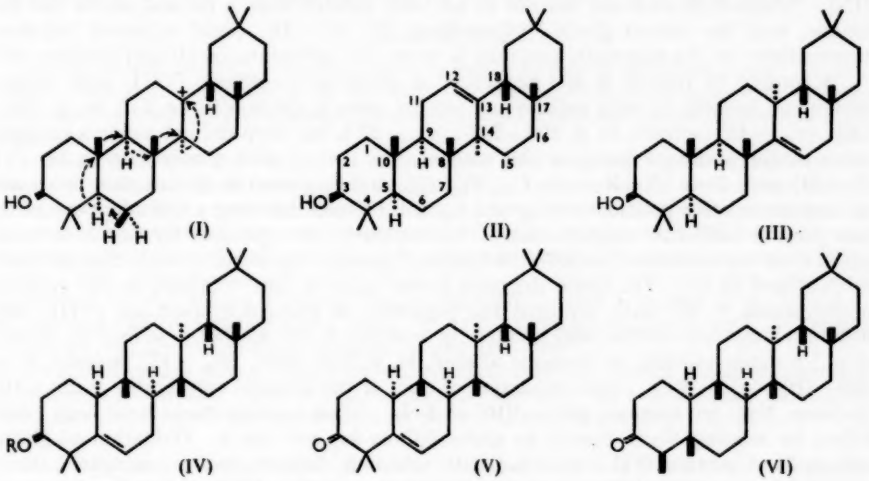
By A. C. PATON, F. S. SPRING, and ROBERT STEVENSON.

Reduction of glutinone (alnusenone) (V) with aluminium *iso*propoxide and *iso*propanol gives a mixture of glutin-5(6)-en-3α- (VII; R = H) and -3β-ol (IV; R = H). Reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride gives a mixture of the epimeric alcohols glutin-5(10)-en-3β- (X; R = H) and -3α-ol (XI; R = H). The configuration of the hydroxyl group in glutin-5(10)-en-3α-ol (XI; R = H) was established by oxidation of its acetate to glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac), previously obtained by similar oxidation of glutin-5(6)-en-3α-yl acetate (VII; R = Ac). Likewise, the configurations of the hydroxyl group in glutin-5(10)- (X; R = H) and -5(6)-en-3β-ol (VI; R = H) were confirmed by the oxidation of the acetates to glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac).

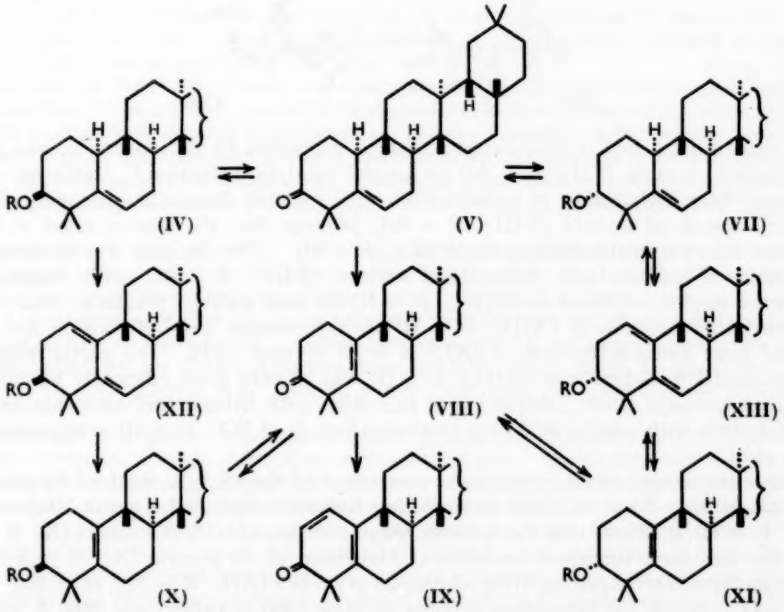
In Part LIV of this series, the constitution and stereochemistry of glutinone (alnusenone) (V) were deduced and were confirmed by partial synthesis from the saturated ketone, friedelin (VI).[1] The biogenesis of friedelin [2] from a squalene-like precursor is considered to proceed *via* the carbonium ion (I) which is also the immediate precursor of β-amyrin (II). Rearrangement of the carbonium ion by a synchronous series or by a succession of 1 : 2-shifts of the axial methyl groups or the axial hydrogen atoms attached at positions 14, 8, 9, 10, 5, and 4, and loss of the hydrogen attached at position 3 as a proton, leads to friedelin [3] (VI). Taraxerol [4] (III) considered to be a stabilised intermediate in this biogenetic route. The biogenesis of glutinone from the carbonium ion (I) is represented as a series of 1 : 2-shifts of the axial methyl groups or axial hydrogen atoms attached at positions 14, 8, 9, 10, and 5 and loss of a proton from $C_{(6)}$. This route, which is illustrated by the arrows in (I), would lead to glutin-5(6)-en-3β-ol (IV; R = H), and the depicted changes are either followed or accompanied by oxidation of the secondary alcohol group. The possible intermediate glutin-5(6)-en-3β-ol (IV; R = H), in which the hydroxyl group is axial, has so far not been isolated from a natural source, but it has now been prepared from glutinone. Reduction of glutinone (V) with lithium aluminium hydride [5, 6] or with sodium and alcohol [5] gives an alcohol (m. p. 203—205°, $[\alpha]_D$ +61°; acetate, m. p. 235—236°, $[\alpha]_D$ +46°) in which the hydroxyl group is equatorial and consequently α-orientated. Oxidation of the alcohol regenerates glutinone and it is therefore identified as glutin-5(6)-en-3α-ol [1] (VII; R = H). We now find that reduction of glutinone (V) with aluminium

[1] Part LIV, Beaton, Spring, Stevenson, and Stewart, *Tetrahedron*, 1958, **2**, 246.
[2] Brownlie, Spring, Stevenson, and Strachan, *J.*, 1956, 2419; Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041; Takahashi and Ourisson, *Bull. Soc. chim. France*, 1956, 353; Dutler, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1268.
[3] Eschenmoser, Ruzicka, Jeger, and Arigoni, *Helv. Chim. Acta*, 1955, **38**, 1890.
[4] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131.
[5] Beaton, Spring, and Stevenson, *J.*, 1955, 2616.
[6] Chapon and David, *Bull. Soc. chim. France*, 1953, 333.

*iso*propoxide and *iso*propyl alcohol gives a mixture which is separated by chromatography on alumina into two homogeneous alcohols. The more strongly adsorbed component of the mixture was recognised as glutin-5(6)-en-3α-ol (VII; R = H). The less strongly



adsorbed component is an isomeric alcohol, $C_{30}H_{50}O$ (m. p. 210·5—211·5°, $[\alpha]_D$ +64°; acetate, m. p. 192—194°, $[\alpha]_D$ +79°). This also is converted into glutinone by oxidation

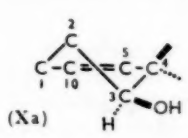


with the chromic acid–pyridine complex and is therefore identified as glutin-5(6)-en-3β-ol (IV; R = H).

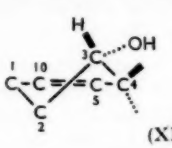
During their study, Beaton *et al.*[1] identified a ketone, obtained by the action of mineral

acid on glutinone,[7] as the isomeric glutin-5(10)-en-3-one (VIII). Its structure follows from the fact that its double bond is tetrasubstituted and that successive treatment with bromine and potassium acetate converts it into a fully conjugated homoannular dienone (IX). Glutin-5(10)-en-3-one has not so far been isolated from a natural source but this ketone, and the related glutin-5(10)-en-3β-ol (X; R = H), could represent stabilised intermediates in the biogenetic pathway between the carbonium ion (I) and friedelin (VI).

According to Beaton *et al.*,[1] reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride or with sodium and alcohol gives a glutin-5(10)-en-3-ol, m. p. 241—242°, $[\alpha]_D$ −42° (acetate, m. p. 290—293°, $[\alpha]_D$ −27°), but they did not assign a configuration to the hydroxyl group in this alcohol. In the epimeric glutin-5(10)-en-3α- (XI; R = H) and -3β-ol (X; R = H), $C_{(1)}$, $C_{(4)}$, $C_{(5)}$, and $C_{(10)}$ must lie in one plane, or nearly so, and the relative positions of $C_{(2)}$ and $C_{(3)}$ will be such that ring A will adopt one of the two possible half-chair conformations. Consequently, it is possible for ring A to adopt a half-chair conformation in which the hydroxyl group is equatorial in each case, as shown in (Xa) and (XIa). The steric situation is the same as that obtaining in the epimeric *neo*ergosterols.[8] We have repeated the reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride and isolated, in addition to the alcohol described by Beaton *et al.*,[1] a minor product, an isomeric alcohol, m. p. 258—259°, $[\alpha]_D$ −42° (acetate, m. p. 209—210°, $[\alpha]_D$ −49°). Since oxidation of each of the alcohols regenerates glutin-5(10)-en-3-one, they are epimeric glutin-5(10)-en-3-ols. Their configurations have been established by relating them directly to glutin-5(6)-en-3α- and -3β-ol. Oxidation of glutin-5(6)-en-3α-yl acetate (VII; R = Ac) with selenium dioxide gives a conjugated dienyl acetate,[1,7] m. p. 164—166°, $[\alpha]_D$ +35°, identified as glutina-1(10) : 5-dien-3α-yl acetate[1] (XIII; R = Ac), which shows absorption maxima at 2300, 2380 (ε 18,000) and 2480 Å.



(Xa)



(XIa)

The structure ascribed to this dienyl acetate is supported by its conversion into glutin-5(6)-en-3α-yl acetate (VII; R = Ac) on partial catalytic reduction.[1] Oxidation of the glutin-5(10)-en-3-yl acetate, m. p. 209—210°, with selenium dioxide likewise gives glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac), proving that the alcohol cited as minor product above is glutin-5(10)-en-3α-ol (XI; R = H). This decision was confirmed by reduction of glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac) with lithium and ammonia to glutin-5(10)-en-3α-ol (XI; R = H) (in poor yield). Similarly, reduction of glutina-1(10) : 5-dien-3α-ol (XIII; R = H) with potassium *tert.*-butoxide in *tert.*-butyl alcohol gave glutin-5(10)-en-3α-ol (XI; R = H) in poor yield. The partial reduction of glutina-1(10) : 5-dien-3α-ol (XIII; R = H) was effected more efficiently by using its tetrahydropyranyl ether. Reduction of this ether with lithium and ammonia followed by hydrolysis with mineral acid gave glutin-5(10)-en-3α-ol (XI; R = H) in approximately 40% yield.

Since the alcohol which is the minor component of the mixture obtained by reduction of glutin-5(10)-en-3-one with lithium aluminium hydride is identified as glutin-5(10)-en-3α-ol (XI; R = H), it follows that the epimeric major component is the 3β-alcohol (X; R = H) and this has been confirmed as follows. Oxidation of its acetate (X; R = Ac) with selenium dioxide gives glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac), m. p. 209—210°, $[\alpha]_D$ +112°, which has absorption maxima at 2310, 2380 (ε 18,000) and 2460 Å and was

[7] Chapon, *Bull. Soc. chim. France.*, 1955, 1076, 1630.
[8] Klyne, "Progress in Stereochemistry," Butterworths Scientific Publications, London, 1954, p. 83.

characterised as the derived alcohol (XII; R = H). Similarly, oxidation of glutin-5(6)-en-3β-yl acetate with selenium dioxide also gave glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac).

Experimental

Rotations refer to $CHCl_3$ and ultraviolet absorption spectra to EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography. M. p.s were determined in open capillaries, except those marked (K) which were determined in the Kofler apparatus.

Glutin-5(6)-en-3β-ol (IV; R = H).—A mixture of glutinone (950 mg.) and aluminium *iso*propoxide (1·25 g.) in absolute *iso*propyl alcohol (12·5 c.c.) was distilled slowly with the addition of *iso*propyl alcohol to maintain constant volume. After 4½ hr., the distillate no longer contained acetone and the solution was evaporated to dryness. The product, isolated in the usual way by means of ether, was chromatographed in light petroleum (30 c.c.) and on alumina (30 g.). Elution with light petroleum–benzene (2 : 1; 1150 c.c.) yielded fractions (246 mg.) which crystallised from chloroform–methanol to give *glutin-5(6)-en-3β-ol* as needles, m. p. (K) 210·5—211·5°, $[\alpha]_D$ +64° (*c* 0·9) (Found: C, 84·2; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). A mixture with glutin-5(6)-en-3α-ol had m. p. (K) 194—196°.

Continued elution with the same solvent mixture (1500 c.c.) yielded mixtures, whereafter light petroleum–benzene (3500 c.c.) gave fractions (460 mg.) which crystallised from chloroform–methanol to yield glutin-5(6)-en-3α-ol, m. p. (K) and mixed m. p. (K) 201—203°, $[\alpha]_D$ +62° (*c* 1·9).

Glutin-5(6)-en-3β-yl Acetate (IV; R = Ac).—Glutin-5(6)-en-3β-ol was treated with pyridine and acetic anhydride at 100° for 90 min. The product, isolated in the usual manner, crystallised from chloroform–methanol, to give *glutin-5(6)-en-3β-yl acetate* as plates, m. p. (K) 192—194°, $[\alpha]_D$ +79° (*c* 1·1), $\lambda_{max.}$ 2050 Å (ε 4050) (Found: C, 82·25; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

Hydrolysis of the acetate (35 mg.) with lithium aluminium hydride (50 mg.) in dry ether (20 c.c.) gave glutin-5(6)-en-3β-ol which crystallised from chloroform–methanol as needles, m. p. (K) and mixed m. p. (K) 210—211°, $[\alpha]_D$ +63° (*c* 0·9).

Oxidation of Glutin-5(6)-en-3β-ol.—The complex from chromium trioxide (100 mg.) and pyridine (1 c.c.) was added to a solution of glutin-5(6)-en-3β-ol (32 mg.) in pyridine (0·5 c.c.) and the mixture kept at room temperature for 17 hr. A solution of the product, isolated in the usual way, in light petroleum (10 c.c.) was filtered through alumina (5 g.), and the column eluted with the same solvent (300 c.c.). The eluate crystallised from chloroform–methanol, to give glutin-5(6)-en-3-one as plates, m. p. (K) and mixed m. p. (K) 244—245°, $[\alpha]_D$ +31° (*c* 1·2).

Glutin-5(10)-en-3β-yl Acetate (X; R = Ac).—Lithium aluminium hydride (450 mg.) was added to a suspension of glutin-5(10)-en-3-one (m. p. 251—253°, $[\alpha]_D$ −91·5°) (750 mg.) in ether (200 c.c.) and kept at room temperature for 1 hr. The product, isolated in the usual way, was treated with pyridine (5 c.c.) and acetic anhydride (5 c.c.) at 100° for 30 min. and the crystals which separated on cooling were collected (mother-liquor A) and recrystallised from chloroform–methanol, to give glutin-5(10)-en-3β-yl acetate (450 mg.) as plates, m. p. (K) 297—299°, $[\alpha]_D$ −23° (*c* 1·7). Beaton *et al.*[1] give m. p. 290—293°, $[\alpha]_D$ −27°, for " alnus-5(10)-en-3ξ-yl acetate."

A suspension of glutin-5(10)-en-3β-yl acetate (55 mg.) in ether (25 c.c.) was treated with lithium aluminium hydride (50 mg.) and refluxed for 5 min. The product was isolated in the usual manner and crystallised from light petroleum from which glutin-5(10)-en-3β-ol separated as needles, m. p. 244—245°, $[\alpha]_D$ −42·5° (*c* 0·8) (Found: C, 84·35; H, 11·5. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%). Beaton *et al.*[1] give m. p. 241—242°, $[\alpha]_D$ −42°, for " alnus-5(10)-en-3ξ-ol."

Glutin-5(10)-en-3α-yl Acetate (XI; R = Ac).—The acetic anhydride–pyridine mother-liquor A (above) was diluted with water and extracted with ether. The extracted solid (225 mg.) crystallised from chloroform–methanol, to give *glutin-5(10)-en-3α-yl acetate* (50 mg.) as needles, m. p. 209—210°, $[\alpha]_D$ −49° (*c* 1·4), $\lambda_{max.}$ 2050 Å (ε 5100) (Found: C, 82·0; H, 11·5. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

Treatment of glutin-5(10)-en-3α-yl acetate with lithium aluminium hydride, and crystallisation of the product from chloroform–methanol, gave *glutin-5(10)-en-3α-ol* as plates, m. p. (K)

258—259°, $[\alpha]_D$ −42° (*c* 1·6), $\lambda_{max.}$ 2060 Å (ε 4300) (Found: C, 83·4; H, 11·9. $C_{30}H_{50}O,\frac{1}{2}MeOH$ requires C, 83·4; H, 11·8%). A mixture with glutin-5(10)-en-3β-ol had m. p. (K) 238—242°.

Glutin-5(10)-en-3-one (VIII).—(*a*) A solution of glutin-5(10)-en-3α-ol (40 mg.) in pyridine (1 c.c.) was added to the chromium trioxide (40 mg.)–pyridine (0·5 c.c.) reagent and kept at room temperature for 15 hr. A solution of the product, isolated in the usual way, in light petroleum was chromatographed on alumina (6 g.). Elution with the same solvent yielded glutin-5(10)-en-3-one as plates (from chloroform–methanol), m. p. (K) and mixed m. p. (K) 251—253°, $[\alpha]_D$ −97° (*c* 1·3). (*b*) Oxidation of glutin-5(10)-en-3β-ol by the method described above gave glutin-5(10)-en-3-one as plates, m. p. (K) and mixed m. p. (K) 251—253°, $[\alpha]_D$ −96° (*c* 1·6).

Glutina-1(10) : 5-*dien*-3α-*yl Acetate* (XIII; R = Ac).—A solution of selenium dioxide (35 mg.) in water (0·1 c.c.) was mixed with one of glutin-5(10)-en-3α-yl acetate (35 mg.) in acetic acid (25 c.c.), and the mixture refluxed for 5 hr. The product, isolated in the usual way, was chromatographed in light petroleum (5 c.c.) on alumina (5 g.). Elution with the same solvent (150 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutina-1(10) : 5-dien-3α-yl acetate as needles, m. p. (K) and mixed m. p. (K) 164—166°, $[\alpha]_D$ +35° (*c* 0·5), $\lambda_{max.}$ 2310 and 2380 Å (ε 15,000 and 17,000), inflexion at 2480 Å (ε 10,000). Beaton *et al.*[1] give m. p. 164—166° $[\alpha]_D$ +35°.

Glutina-1(10) : 5-*dien*-3α-*ol* (XIII; R = H).—Treatment of the dienyl acetate with lithium aluminium hydride and crystallisation of the product from chloroform–methanol gave glutina-1(10) : 5-dien-3α-ol as prismatic needles, m. p. (K) and mixed m. p. (K) 198—200°, $[\alpha]_D$ +84° (*c* 1·6), $\lambda_{max.}$ 2330 and 2400 Å (ε 16,000 and 18,000), inflexion at 2480 Å (ε 11,000). Beaton *et al.*[1] give m. p. 195—197°, $[\alpha]_D$ +83°.

Glutina-1(10) : 5-*dien*-3β-*yl Acetate* (XII; R = Ac).—(*a*) A solution of selenium dioxide (100 mg.) in water (0·1 c.c.) was mixed with a solution of glutin-5(10)-en-3β-yl acetate (100 mg.) in acetic acid (50 c.c.). After 3 hours' refluxing, the solvent was removed and a solution of the product in light petroleum (10 c.c.) was chromatographed on alumina (8 g.). Crystallisation of the fractions eluted by light petroleum (175 c.c.) from chloroform–methanol gave *glutina*-1(10) : 5-*dien*-3β-*yl acetate* as plates (75 mg.), m. p. 209—210°, $[\alpha]_D$ +112° (*c* 1·0), $\lambda_{max.}$ 2310, 2380, and 2460 (inflex.) Å (ε 16,500, 18,000, and 11,000) (Found: C, 82·3; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). It gives a deep orange colour with tetranitromethane. (*b*) Glutin-5(6)-en-3β-yl acetate (80 mg.) in acetic acid (20 c.c.) was treated with a solution of selenium dioxide (80 mg.) in water (0·1 c.c.) and acetic acid (2 c.c.), and kept at 60—70° for 1 hr. The filtered solution was evaporated to dryness and a solution of the residue in light petroleum (5 c.c.) chromatographed on alumina (10 g.). Elution with the same solvent (750 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutina-1(10) : 5-dien-3β-yl acetate as blades (68 mg.), m. p. (K) and mixed m. p. (K) 209—210°, $[\alpha]_D$ +112·5° (*c* 1·1), $\lambda_{max.}$ 2320 and 2380 Å (ε 15,000 and 16,500), inflexion at 2470 Å (ε 10,000).

Glutina-1(10) : 5-*dien*-3β-*ol* (XII; R = H).—A solution of the dienyl acetate (40 mg.) in ether (15 c.c.) was refluxed with lithium aluminium hydride (100 mg.) for 30 min. The product, in light petroleum–benzene (2 : 1; 15 c.c.), was chromatographed on alumina (5 g.), and the fraction eluted by benzene–ether (20 : 1; 100 c.c.), crystallised from methanol, to give *glutina*-1(10) : 5-*dien*-3β-*ol* as needles, m. p. (K) 195—197°, $[\alpha]_D$ +110° (*c* 0·6), $\lambda_{max.}$ 2320, 2390, and 2470 (inflex.) Å (ε 15,000, 16,000, and 10,000) (Found: C, 84·9; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%).

3α-2′-*Tetrahydropyranyloxyglutina*-1(10) : 5-*diene*.—Toluene-*p*-sulphonic acid (0·5 mg.) was added to a solution of glutina-1(10) : 5-dien-3α-ol (350 mg.) in benzene (15 c.c.) and dihydropyran (1·5 c.c.), and the mixture kept at room temperature for 16 hr. A solution of the product, isolated in the usual way, in light petroleum (40 c.c.) was chromatographed on alumina (30 g.). The fractions eluted by light petroleum (300 c.c.) were crystallised from chloroform–methanol, to give 3α-2′-*tetrahydropyranyloxyglutina*-1(10) : 5-*diene* as needles (after gelation), m. p. (K) 171—173°, $[\alpha]_D$ +70° (*c* 1·6), $\lambda_{max.}$ 2340 (inflex.), 2400, and 2380 (inflex.) Å (ε 13,500, 14,500, and 9600) (Found: C, 82·9; H, 11·3. $C_{35}H_{56}O_2$ requires C, 82·6; H, 11·1%).

Glutin-5(10)-en-3α-ol (XI; R = H).—(*a*) Lithium (300 mg.) was added to a solution of 3α-2′-tetrahydropyranyloxyglutina-1(10) : 5-diene (285 mg.) in ether (150 c.c.) and liquid ammonia (300 c.c.), and the mixture stirred for 1 hr. Ethanol (10 c.c.) was added and the product, isolated in the usual way, was refluxed in benzene (10 c.c.), ethanol (20 c.c.), and concentrated hydrochloric acid (0·25 c.c.) for 90 min.; the hydrolysed product was then

chromatographed in light petroleum (20 c.c.) on alumina (10 g.). Elution with light petroleum–benzene (1 : 6; 425 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutin-5(10)-en-3α-ol as plates (95 mg.), m. p. (K) and mixed m. p. (K) 258—259°, $[\alpha]_D$ −42° (*c* 1·6), $\lambda_{max.}$ 2040 Å (ε 4300). This alcohol with pyridine and acetic anhydride at 100° gave its acetate as needles, m. p. (K) and mixed m. p. (K) 209—210°, $[\alpha]_D$ −49° (*c* 1·4).

(*b*) Lithium (150 mg.) was added to a solution of glutina-1(10) : 5-dien-3α-yl acetate (100 mg.) in ether (50 c.c.) and liquid ammonia (100 c.c.), and the mixture stirred for 1 hr. After addition of ethanol (10 c.c.), the ammonia was allowed to evaporate. The product, isolated in the usual way, was acetylated with pyridine and acetic anhydride and chromatographed on alumina (10 g.). Elution with light petroleum (175 c.c.) yielded a fraction (15 mg.) which after three recrystallisations from chloroform–methanol gave glutin-5(10)-en-3α-yl acetate as needles, m. p. (K) and mixed m. p. (K) 207—208°, $[\alpha]_D$ −48° (*c* 0·3).

(*c*) Potassium (6·5 g.) was added to a solution of glutina-1(10) : 5-dien-3α-ol (100 mg.) in *tert.*-butyl alcohol (100 c.c.), the mixture was heated at 100° for 18 hr., then diluted with water, and the product was isolated in the usual way and chromatographed in light petroleum–benzene (9 : 1; 15 c.c.) on alumina (10 g.). Elution with this solvent mixture (125 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutin-5(10)-en-3α-ol as plates (12 mg.), m. p. 247—251°, $[\alpha]_D$ −36° (*c* 0·7), raised to m. p. (K) and mixed m. p. (K) 254—256° on recrystallisation. A mixture of the alcohol and glutin-5(10)-en-3β-ol had m. p. 235°.

One of us (A. C. P.) thanks the Department of Scientific and Industrial Research for the award of a Research Studentship.

THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
GLASGOW.

[*Received, December 27th*, 1957.]

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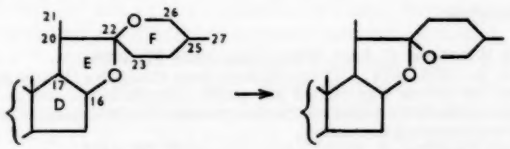
543. *Steroidal Sapogenins: The Isomerisation of Normal to* iso-*Sapogenins.*

By R. K. CALLOW and (MISS) P. N. MASSY-BERESFORD.

Support for a hypothesis of the mechanism of the isomerisation by acid of " normal " sapogenins (25*L*) into " *iso* "-sapogenins (25*D*) has been obtained by effecting the change with deuterium ions, followed by location of the deuterium in the isomerisation product by degradation. The reversibility of the isomerisation has been confirmed, and it has been shown that, under the conditions for inversion at position 25, deuterium–hydrogen exchange also occurs at position 20.

MARKER and ROHRMANN [1] reported the conversion, by prolonged treatment with 2N-ethanolic hydrochloric acid of the " normal " sapogenin sarsasapogenin into the " *iso* "-sapogenin smilagenin, and suggested that the reaction involves the opening and reclosure of the terminal oxide ring:



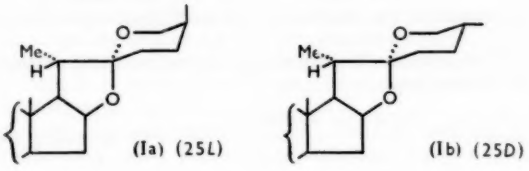
" Normal " sapogenin → " *Iso* "-Sapogenin

The isomerisation is a general reaction of the " normal " sapogenins.

[1] Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1939, **61**, 846.

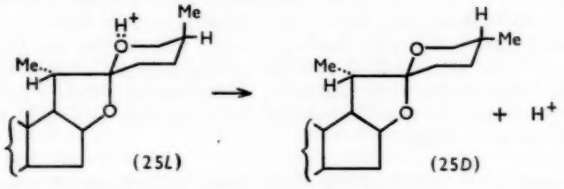
Further investigation [2] of the isomerisation of sarsasapogenin showed that the reaction yields a mixture containing sarsasapogenin, smilagenin, and the corresponding Δ^2- or Δ^3-3-deoxysapogenins, and also that the isomerisation is an equilibration in which the formation of the more stable "*iso*"-sapogenin is favoured.

Callow and James [3] investigated alternative conditions of isomerisation and found that the reaction takes place in hot dioxan containing hydrochloric acid, and also occurs in the presence of acetic anhydride under similar, anhydrous conditions, so that the change must take place without the opening of ring F. Scheer, Kostic, and Mosettig [4] showed that the "normal" and the "*iso*"-sapogenins differ in configuration at position 25; James [5] related the configuration at this asymmetric centre to glyceraldehyde, and it has been proved [6] that *neo*tigogenin (25*L*) and tigogenin (25*D*) have the same configuration at all asymmetric centres except $C_{(25)}$. The absolute configuration at $C_{(22)}$ has been discussed [6] and structures (Ia) and (Ib) have been proposed for the 25*L*- and the 25*D*-sapogenins. It must follow that the isomerisation (Ia) ⟶ (Ib) consists of an inversion of configuration at $C_{(25)}$, in which the methyl group attached to $C_{(25)}$ changes from the axial to the equatorial conformation.



Cornforth [7] suggested that the inversion occurs by the addition of a proton to the oxygen atom of ring F of the 25*L*-sapogenin, the proton then being well placed to initiate a displacement reaction with inversion of configuration at $C_{(25)}$.

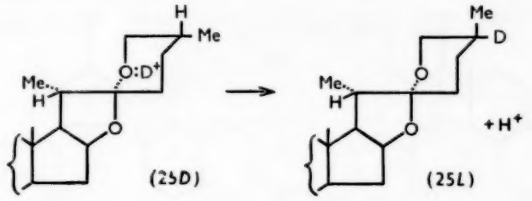
If the isomerisation takes place by this process, treatment of a 25*L*-sapogenin with deuterium ions should give a 25*D*-sapogenin containing, at position 25, one deuterium atom stable towards brief treatment with acids.[8] Proof of the position of the deuterium should be obtainable by degradation. If the isomerisation is reversible,[2] similar treatment of a



25*D*-sapogenin with deuterium ions should also introduce deuterium at position 25. This reverse process could occur by a mechanism similar to that suggested by Cornforth if the sapogenins can exist with ring F in the less stable [9] "upright" conformation under the conditions of isomerisation.

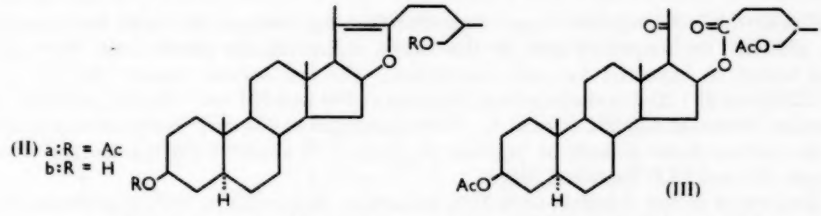
[2] Wall, Serota, and Witnauer, *J. Amer. Chem. Soc.*, 1955, **77**, 3086.
[3] Callow and James, *J.*, 1955, 1671. [It should have been made clear in this paper that the reaction in the presence of acetic anhydride was carried out under anhydrous conditions, with dioxan (10 ml.) saturated with hydrogen chloride in place of the concentrated hydrochloric acid (15 ml.) used in the experiment described immediately previously.]
[4] Scheer, Kostic, and Mosettig, *J. Amer. Chem. Soc.*, 1953, **75**, 4871.
[5] James, *J.*, 1955, 637.
[6] Callow and Massy-Beresford, *J.*, 1957, 4482.
[7] Cornforth, *Ann. Reports*, 1953, **50**, 219.
[8] Callow, James, and Massy-Beresford, *Chem. and Ind.*, 1956, R26.
[9] Hirschmann, Hirschmann, and Corcoran, *J. Org. Chem.*, 1955, **20**, 572.

It was found that *neo*tigogenin acetate (25*L*) was isomerised when heated in a sealed tube on the steam-bath for 55 hr. with 6·5 molecular proportions of 1·4N-deuterium chloride in dioxan. After treatment of the product with boiling acetic acid [8] or 0·5N-methanolic hydrochloric acid to remove labile deuterium, and alkali-treatment to complete



saponification of the acetate group, deuterated tigogenin containing 1·0 D (where the symbol D signifies gram-atoms of deuterium per mole of steroid) was obtained in 50% yield. The same product was obtained by similar treatment of tigogenin acetate in full accordance with the assumed reversibility of the isomerisation. The deuterated tigogenin showed weak carbon–deuterium stretching absorption bands in the infrared spectrum at 2175 and 2130 cm.$^{-1}$, and the spectrum differed from that of tigogenin in the " fingerprint " region, especially in that the 915 cm.$^{-1}$ band was more intense than the band at 895 cm.$^{-1}$.

It was originally intended to determine the position of the deuterium by oxidative degradation of the corresponding *pseudo*sapogenin, followed by isolation and degradation of the side-chain. A method of isolation of the side-chain without oxidation at position 26 was devised using unlabelled starting material. Oxidation of *pseudo*tigogenin diacetate (IIa) by chromic acid at room temperature gave 3β-acetoxy-16β-(δ-acetoxy-γ-methylvaleroyloxy)-5α-pregnan-20-one (III), which, on methanolysis with N-hydrogen chloride in dry methanol, yielded a mixture of methyl δ-hydroxy-γ-methylvalerate (IV), a γ-lactone,



(IV) HO·CH$_2$·CHMe·CH$_2$·CH$_2$·CO$_2$Me HO·CH$_2$·CHMe·CH$_2$·CH$_2$·CO·NH·CHPh$_2$ (V)

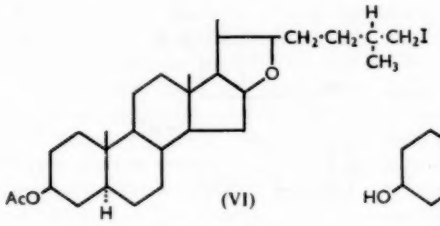
and a δ-lactone. Treatment of the mixture with diphenylmethylamine yielded the crystalline amide (V) of δ-hydroxy-γ-methylvaleric acid. When the process was repeated with deuterated tigogenin (1·0 D), the mixture containing the methyl ester was found to contain only 0·13 D and did not yield a crystalline diphenylmethylamide. This method of degradation was abandoned when another approach proved successful.

Sato and Latham [10] reported the conversion of tigogenin into 3β-acetoxy-16 : 22-epoxy-26-iodocholestane (VI); this was unstable, being extremely sensitive to treatment with alkali,[11] which caused simultaneous deacetylation and dehydrohalogenation to give 16 : 22-epoxycholest-25-en-3β-ol (VII). This reaction suggested a method of determining the position of the deuterium in deuterated tigogenin, since a deuterium atom at position 25 would be completely removed by dehydroiodination of a 26-iodo-derivative.

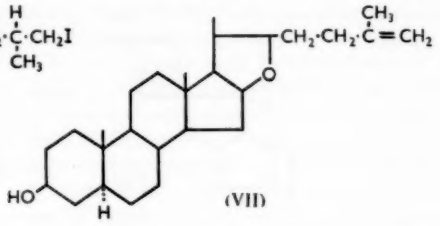
[10] Sato and Latham, *J. Amer. Chem. Soc.*, 1956, **78**, 3150.
[11] Sato, Latham, and Scheer, *J. Org. Chem.*, 1956, **21**, 689.

XUM

Tigogenin was converted into dihydrotigogenin (VIIIa) in high yield by catalytic hydrogenation with a trace of perchloric acid as a promoter.[12] Dihydrotigogenin was converted into the ditoluene-*p*-sulphonate (VIIIb) which on treatment with sodium iodide in ethyl methyl ketone gave **16 : 22-epoxy-3ξ : 26-di-iodocholestane** (IX), a stable, highly

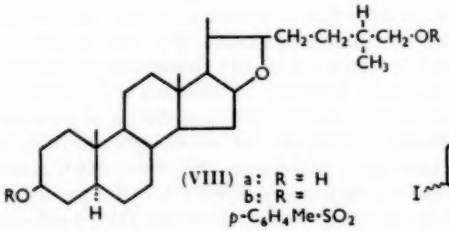


(VI)

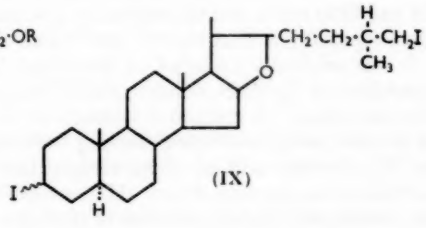


(VII)

crystalline solid, in 52% yield. Fractional crystallisation indicated that two isomers were present which differed in solubility, crystalline form, melting point, and infrared absorption spectrum both in the solid state and in CS_2 solution. Analysis of the infrared absorption



(VIII) a: R = H
b: R = *p*-$C_6H_4Me{\cdot}SO_2$



(IX)

spectra in the low-frequency range suggested that the compounds might be isomeric at $C_{(3)}$, although the frequency shift for the carbon–iodine linkage (about 2 cm.$^{-1}$) is smaller than would be expected for such isomerism. The less soluble isomer, thought to be **16 : 22-epoxy-3β : 26-di-iodocholestane**, absorbs at **680** and **604** cm.$^{-1}$ (in CS_2 solution), and the other isomer at **678** and **604** cm.$^{-1}$. The absorption at **604** cm.$^{-1}$ is tentatively assigned to the carbon–iodine linkage at position 26, since it is absent from the spectra of compounds (X) and (XI) described below.

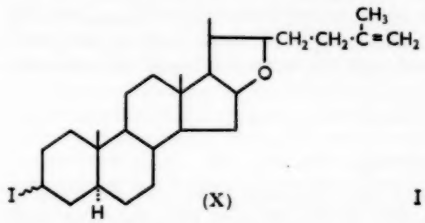
Treatment of the di-iodide with 10% potassium hydroxide in boiling ether–methanol yielded a **4 : 1** mixture, separable by chromatography, of **16 : 22-epoxy-3ξ-iodocholest-25-ene** (X) and **16 : 22-epoxy-3ξ-iodo-26-methoxycholestane** (XI). Both compounds were stable crystalline solids.

This series of reactions was repeated with deuterated tigogenin (0·9 D) (prepared from *neo*tigogenin acetate by isomerisation with deuterium chloride), which gave deuterated dihydrotigogenin (0·8 D), the ditoluene-*p*-sulphonate (0·8 D), and deuterated **16 : 22-epoxy-3ξ : 26-di-iodocholestane** containing 0·95 D. Dehydroiodination gave **16 : 22-epoxy-3ξ-iodocholest-25-ene** which unexpectedly contained **0·46** D. Evidently only half the deuterium content of the deuterated tigogenin had been situated at position **25**. That the remainder was situated at position 20 was proved by the following series of experiments in which specific measures designed to remove deuterium from position 20, by introduction of the **20 : 22-double** bond, were taken.

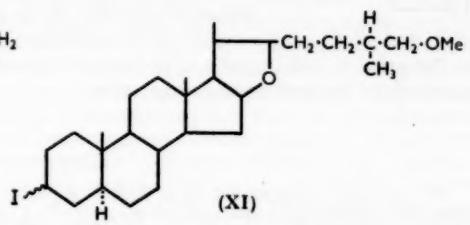
Since further supplies of *neo*tigogenin were not available, advantage was taken of the reversibility of the isomerisation and tigogenin acetate was used for the preparation of

[12] Hershberg, Oliveto, Rubin, Staeudle, and Kuhlen, *J. Amer. Chem. Soc.*, 1951, **73**, 1144.

deuterated tigogenin. The amount of 1·4N-deuterium chloride used in the reaction (12·5 molecular proportions) was twice that employed in previous experiments. After removal of labile deuterium and purification, the deuterated tigogenin containing 1·56 D. This was converted into deuterated *pseudo*tigogenin (IIb) contained 0·6 D, which was cyclised by acid to give deuterated tigogenin containing 0·48 D. The infrared absorption spectrum of this compound showed a single C–D stretching band at 2120 cm.$^{-1}$, and differed from that of tigogenin in the " fingerprint " region, having three bands of equal intensity



(X)

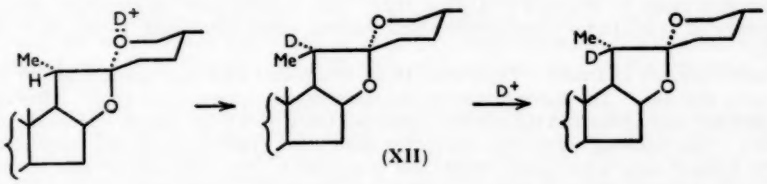


(XI)

at 920, 896, and 885 cm.$^{-1}$, and no absorption at 865 cm.$^{-1}$. The deuterated tigogenin was converted into deuterated 16 : 22-epoxy-3ξ : 26-di-iodocholestane (0·47 D), which was dehydroiodinated to give 16 : 22-epoxy-3ξ-iodocholest-25-ene that contained no detectable deuterium.

These results support the hypothesis that the isomerisation of the sapogenins is a reversible reaction which proceeds by the mechanism suggested by Cornforth.[7] In addition it has been shown that deuterium–hydrogen exchange occurs at position 20 under the conditions for inversion at $C_{(25)}$, since deuterated tigogenin (1·56 D) loses one deuterium atom when converted, by introduction of the 20 : 22-double bond, into deuterated *pseudo*-tigogenin (0·6 D).

This exchange at position 20 could occur by two alternative processes. When a deuteron adds to the oxygen atom of ring F, it is equally well placed to cause displacement with inversion at either $C_{(25)}$ or $C_{(20)}$. Inversion at $C_{(20)}$ would give the 20-*iso*sapogenin (XII) with the 20-methyl group in the hindered β-position. These isomers are



(XII)

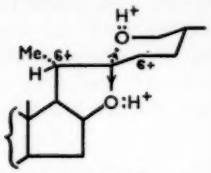
obtained [13-15] by very mild acid treatment of *pseudo*sapogenins, and are readily converted into 20α-sapogenins by further acid treatment. If a 20β-sapogenin were formed during the isomerisation, it would be converted immediately into the 20α-isomer in the presence of 1·4N-deuterium chloride.

An alternative and more probable explanation is that the spiroketal group causes activation of the hydrogen atom at $C_{(20)}$ towards deuterodeprotonation. The well-known reactivity of position 23 of the sapogenins under acid conditions is thought to result from the addition of protons to the oxygen atoms of rings E and F, which causes an electron deficiency at $C_{(23)}$ by electromeric changes *via* the spiroatom as indicated in the diagram.

[13] Callow, Dickson, Elks, Evans, James, Long, Oughton, and Page, *J.*, 1955, 1966.
[14] Wall, Serota, and Eddy, *J. Amer. Chem. Soc.*, 1955, **77**, 1230.
[15] Ziegler, Rosen, and Shabica, *ibid.*, 1954, **76**, 3865.

XUM

Similar activation of the hydrogen atom at $C_{(20)}$ must also occur, but is probably somewhat reduced by the inductive effect of the 20-methyl group. The exchange which occurs [8] when the sapogenins are boiled with deuterium acetate is thought to occur at position 23. Deuterium at position 23 is readily removed by brief treatment with acids, but the deuterium introduced at position 20 by deuterium chloride in hot dioxan is evidently stable to brief acid treatment. This must be due partly to steric effects, since the deuterium atom at $C_{(20)}$ is shielded by the 20α- and the 13β-methyl group, partly to the reduced activation at $C_{(20)}$ compared with that at $C_{(23)}$ as a result of the inductive effect of the 20-methyl group, and partly to the greater stability of a C–D bond compared with the corresponding C–H bond which is a result of the deuterium isotope effect.



Experimental

M. p.s were determined in a Kofler apparatus with polarised light, and are corrected. Optical rotations were determined for $CHCl_3$ solutions of concentration 1·0% unless otherwise stated. Samples for analysis were recrystallised to constant m. p., and in the case of dihydrotigogenin and tigogenin were dried for 8 hr. in a slow stream of air at 100° and 140° respectively. For deuterated compounds, the percentages of hydrogen found are " apparent " since they were computed as though the water formed was pure H_2O. The required values given for comparison have been calculated in the same way, and all " apparent " values for hydrogen are designated by " H ". Infrared absorption was measured with a double-beam instrument with a rock-salt prism (Perkin-Elmer Model 21) in KCl discs unless otherwise stated.

Deuterium Analyses.—The percentage of deuterium oxide in the water formed by combustion of a sample (30—60 mg.) of deuterated steroid was determined by infrared analysis, by a method derived from those described by Trenner and Walker,[16] and Berglund-Larsson.[17] The HOD absorption at 2500 cm.$^{-1}$ of a film of the water sample was determined in a cell made of two crystalline quartz plates 0·5 mm. in thickness, separated by aluminium foil strips 0·017 mm. in thickness. The absorption of the empty cell was balanced by that of two similar quartz plates in the compensating beam. The slit width was 30 μ. For each analysis, a calibration curve was recorded by using solutions of D_2O in H_2O of known concentration, and the concentration of the unknown was determined by interpolation of the plot of the logarithm of the percentage of D_2O against the percentage absorption at 2500 cm.$^{-1}$, which is a straight line over the concentration range 1—8% w/w of D_2O in H_2O. The method gave reproducible results with an accuracy of ±0·1 D for compounds which yielded water containing 1—8% w/w of D_2O in H_2O.

pseudo*Tigogenin Diacetate.*—Tigogenin (10 g.) was boiled with *n*-octanoic acid (20 ml.) for 2 hr. under nitrogen. The water formed in the reaction was collected in a trap. After cooling, ether (200 ml.) was added and the solution extracted twice with 0·5N-sodium hydroxide solution (300 ml.). The aqueous layers were extracted with ether (100 ml.), and the combined ether extracts washed once with water, dried, and evaporated. The residual oil was boiled with 5% potassium hydroxide in methanol for 30 min. Hot water (~800 ml.) was added slowly to the hydrolysis solution. After cooling, the solid was collected, washed with hot, slightly alkaline water, and dried *in vacuo* over sodium hydroxide.

The crude *pseudo*tigogenin (7·6 g.) was acetylated in pyridine–acetic anhydride (1 : 1) on the steam-bath for 30 min. The solvents were evaporated under reduced pressure and the residue was dissolved in carbon tetrachloride and evaporated to dryness six times. The gummy diacetate was used for the next stage without further purification.

3β-*Acetoxy*-16β-(δ-*acetoxy*-γ-*methylvaleroyloxy*)-5α-*pregnan*-20-*one.*—A solution of chromic oxide (7·5 g.) in 80% acetic acid (75 ml.) was added to a solution of *pseudo*tigogenin diacetate in glacial acetic acid (75 ml.) at 30°. The temperature rose to 49°, and the mixture was stirred at room temperature for 1½ hr. Ethanol (5 ml.) was added, and the mixture was poured into water, saturated with sodium chloride, and extracted with ether. The extract was washed

[16] Trenner and Walker, *Perkin-Elmer Instrument News*, 1952, **4**, No. 1.
[17] Berglund-Larsson, *Acta Chem. Scand.*, 1956, **10**, 701.

with sodium hydrogen carbonate solution until free from acid, then with water, dried and evaporated.

N-Diphenylmethyl-δ-hydroxy-γ-methylvaleramide.—The oxidation product (7·85 g.) was boiled with N-hydrogen chloride in dry methanol (70 ml.) for 3 hr. and left overnight at room temperature. The solution was adjusted to pH 6 with 1·88N-potassium hydroxide in methanol (25·5 ml.), and the solvent was evaporated under reduced pressure at room temperature. The gum was dissolved in ether, which was then dried ($MgSO_4$) and filtered to remove inorganic salts. The filtrate was evaporated under reduced pressure at the lowest possible temperature. The residual gum was heated slowly under reduced pressure to 130°. A distillate was obtained, infrared examination of which indicated that it was a mixture of a methyl ester, a γ-lactone, and a δ-lactone, which were not separated by fractional distillation. The combined fractions (600 mg.) were dissolved in dry benzene (25 ml.), diphenylmethylamine (2·0 g.) was added, and the solution boiled for 18 hr. with the exclusion of atmospheric carbon dioxide. The benzene was evaporated under reduced pressure and the residue treated with aqueous orthophosphoric acid. The precipitate was collected, washed with aqueous orthophosphoric acid, and dried *in vacuo* over P_2O_5. The solid (500 mg.) was crystallised twice from benzene, to give needles of *N-diphenylmethyl-δ-hydroxy-γ-methylvaleramide*, m. p. 118—119°, $[\alpha]_D$ +8° (Found: C, 77·0; H, 7·8; N, 4·8. $C_{19}H_{23}O_2N$ requires C, 76·7; H, 7·8; N, 4·7%), $\nu_{max.}$ 3275, 3020, 2920, 2840, 1647, 1534, 1500, 1245, 1227, 1040, 980, 753, 738, 695 cm.$^{-1}$, $\nu_{max.}$ (in CCl_4) 3270, 3010 (w), 2900, 2840, 1645, 1500, 1040, 690 cm.$^{-1}$.

Dihydrotigogenin.—Tigogenin acetate (2·0 g.) in glacial acetic acid (200 ml.) containing 3 drops of 72% perchloric acid was hydrogenated over platinum oxide (300 mg.) at room temperature and 32 lb./sq. in. for 18 hr. The catalyst was removed and the filtrate diluted with water, neutralised with 50% sodium hydroxide solution, and extracted with ether. The ether extract was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The residue was boiled with 3% potassium hydroxide in methanol for 1 hr. The solution was poured into water and neutralised, and the solid collected, washed, and dried (1·64 g., 90%). Dihydrotigogenin had m. p. 167—171° (from acetone), $[\alpha]_D$ −4° (Found: C, 77·0; H, 11·0. Calc. for $C_{27}H_{46}O_3$: C, 77·5; H, 11·1%) (lit.,[18] m. p. 163—166°, $[\alpha]_D$ −4°).

Dihydrotigogenin 3β : 26-*Ditoluene*-p-*sulphonate.*—Dihydrotigogenin (1·18 g., 2·8 mmoles) was dissolved in pyridine (15 ml.) (which had been dried, distilled, and kept over barium oxide) and cooled to −10°. Toluene-*p*-sulphonyl chloride (3·6 g., 19 mmoles) was added and the mixture swirled, with cooling, until the acid chloride had dissolved. The solution was kept at 0° for 2 hr. and at room temperature overnight. Ice was added, and after 30 min. the mixture was extracted with ether. The extract was washed well with cold N-hydrochloric acid, with water, with 2% sodium hydrogen carbonate solution, and with water, dried, and evaporated under reduced pressure. The gummy product (1·97 g., 96%) had no infrared absorption due to hydroxyl, but bands at 1710 (m), 1595 (aromatic C=C); 1365, 1185, 1170 (S=O stretching); 1090, 925, 860, 835, 805, 660 cm.$^{-1}$, and was used for the next stage without further purification.

16 : 22-*Epoxy*-3ξ : 26-*di-iodocholestane.*—Dihydrotigogenin 3β : 26-di-*p*-toluenesulphonate (1·97 g.) was dissolved in ethyl methyl ketone (50 ml.), sodium iodide (4·0 g.) was added, and the mixture boiled for 17 hr. After cooling, the insoluble salts were filtered off, the solvent was evaporated under reduced pressure at room temperature, and the residue partitioned between chloroform and water. The chloroform layer was washed with sodium thiosulphate solution and water, dried, and evaporated under reduced pressure at room temperature. On treatment of the residual gum with ether, white crystals were obtained (739 mg., 52% from dihydrotigogenin). The product was crystallised twice from ether–methanol, to give plates of 16 : 22-*epoxy*-3(β?) : 26-*di-iodocholestane*, m. p. 140—146°, $[\alpha]_D$ +6° (Found: C, 50·9; H, 6·8; I, 39·6. $C_{27}H_{44}OI_2$ requires C, 50·8; H, 7·0; I, 39·8%), $\nu_{max.}$ 1145, 1105, 1050, 990, 670, 640 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 680, 650, 604 cm.$^{-1}$. A more soluble *isomer* was obtained from the mother-liquors as needles, m. p. 146—151°, $[\alpha]_D$ +6° (Found: C, 51·1; H, 7·2; I, 39·0%), $\nu_{max.}$ 1173, 1047, 672, 640 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 678, 604, 475 cm.$^{-1}$.

16 : 22-*Epoxy*-3ξ-*iodocholest*-25-*ene.*—16 : 22-Epoxy-3ξ : 26-di-iodocholestane (500 mg.) was dissolved in ether (50 ml.). A solution of potassium hydroxide (15 g.) in methanol (150 ml.) was added, some of the ether was evaporated, and the solution boiled for 6 hr., poured into water, cooled, and extracted with ether. The extract was washed with water, dried, and evaporated

[18] Doukas and Fontaine, *J. Amer. Chem. Soc.*, 1951, **73**, 5917.

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under reduced pressure at room temperature. The residue (397 mg.) was chromatographed on alumina (Spence Type H). Benzene–light petroleum (b. p. 60—80°) (1 : 4) eluted material (324 mg., 81% from the di-iodide) which was crystallised from ethanol to give needles of **16 : 22-*epoxy*-3ξ-*iodocholest*-25-*ene***, m. p. 92—95°, $[\alpha]_D$ +7° (*c* 0·62%) (Found: C, 63·9; H, 8·7; I, 24·5. $C_{27}H_{43}OI$ requires C, 63·5; H, 8·5; I, 24·9%), $\nu_{max.}$ 3020 (w), 1650, 1110, 882, 675, 640 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 1650 and 885 (>C=CH_2), 681 cm.$^{-1}$.

Benzene–light petroleum (b. p. 60—80°) (2 : 3) eluted **16 : 22-*epoxy*-3ξ-*iodo*-26-*methoxycholestane*** (57 mg., 13·4% from the di-iodide), m. p. 124—131° (plates from acetone), $[\alpha]_D$ +6° (*c* 0·7%) (Found: C, 62·1; H, 8·7; I, 23·1; MeO, 6·5. $C_{28}H_{47}O_2I$ requires C, 62·0; H, 8·7; I, 23·4; MeO, 5·7%), $\nu_{max.}$ 1110 (s), 676, 640 cm.$^{-1}$, $\nu_{max.}$ (in CS_2) 1108 (C·OMe), 680 cm.$^{-1}$.

Preparation of a Solution of Deuterium Chloride in Dioxan.—A mixture of phosphorus pentachloride (62·5 g., 0·3 mole) and phosphorus oxychloride (70 ml.) was cooled in an ice-bath in a flask equipped with a dropping funnel, stirrer, inlet tube leading into the solution, and an outlet lead. The outlet lead was connected to a cold-trap cooled in alcohol–carbon dioxide, and this was connected to a flask containing pure dioxan (75 ml.) equipped with inlet lead, condenser, and calcium chloride guard tube. A slow stream of nitrogen was passed through the apparatus, and deuterium oxide (6·02 g., 0·3 mole) was added slowly from the dropping funnel. After the addition, stirring was continued for 30 min. and nitrogen was passed through the apparatus. The resulting solution of deuterium chloride in dioxan was found by titration to be 4·79N (yield 60% from deuterium oxide).

Isomerisation of neo*Tigogenin Acetate with Deuterium Chloride.*—*neo*Tigogenin acetate (2·0 g., 4·36 mmoles) was dissolved in dioxan (10 ml.) in a Carius tube. The solution was frozen, the tube was flushed with nitrogen, and 2·85N-deuterium chloride in dioxan (10 ml., 28·5 mmoles) was added. The tube was sealed and heated on the steam-bath for 60 hr. After cooling, the solution was poured into sodium carbonate solution, and the solid collected, washed, and dried. The crude product (1·98 g.) was dissolved in methanol (100 ml.), concentrated hydrochloric acid (5 ml.) was added, and the solution boiled for 30 min., then poured into water. The solid was collected, washed, and dried. The partially acetylated product was boiled in methanol containing 2% of potassium hydroxide for 1 hr., the solution was poured into water, and the solid collected, washed, and dried. The product (1·93 g.) was allowed to percolate through neutral alumina in benzene solution to remove coloured impurities and crystallised from methanol. The ***deuterated tigogenin*** had m. p. 195—199°, $[\alpha]_D$ −71° (Found: C, 77·7; " H ", 10·8; 0·98 D. $C_{27}H_{43}DO_3$ requires C, 77·7; " H ", 10·6%), $\nu_{max.}$ 2175 (w) and 2130 (w) (C−D stretching), 915 > 895, 870 (m) cm.$^{-1}$.

Deuterated Tigogenin from Tigogenin Acetate.—Treatment of tigogenin acetate (13 g., 28·3 mmoles) with 1·4N-deuterium chloride (350 mmoles) as described above yielded crude material containing 3·1 D. After treatment with 0·5N-methanolic hydrochloric acid, chromatography, and crystallisation from ether the deuterated tigogenin had m. p. 189—195°, $[\alpha]_D$ −64° (*c* 0·69%) (Found: C, 77·6; " H ", 10·5; 1·56 D), $\nu_{max.}$ 2170 (w), 2120 (w) cm.$^{-1}$.

Conversion of Deuterated Tigogenin into Deuterated **16 : 22-*Epoxy*-3ξ-*iodocholest*-25-*ene***.—Deuterated tigogenin (0·9 D) prepared from *neo*tigogenin acetate was converted, by the methods described previously, into ***deuterated dihydrotigogenin***, m. p. 165—170° (from acetone), $[\alpha]_D$ −5° (*c* 1·2%) (Found: C, 77·2; " H ", 11·3; 0·8 D. $C_{27}H_{45}DO_3$ requires C, 77·3; " H ", 11·1%). This was converted into the ditoluene-*p*-sulphonate (0·8 D) which was then converted into ***deuterated*** **16 : 22-*epoxy*-3ξ : 26-*di*-*iodocholestane***, m. p. 142—146° (from ether–methanol), $[\alpha]_D$ +6° (Found: C, 51·0; " H ", 6·7; I, 39·1; 0·95 D. $C_{27}H_{43}DOI_2$ requires C, 50·7; " H ", 7·0; I, 39·7%). Dehydroiodination gave ***deuterated*** **16 : 22-*epoxy*-3ξ-*iodocholest*-25-*ene***, m. p. 93—96° (from ethanol), $[\alpha]_D$ +7° (*c* 0·74%) (Found: C, 63·3; " H ", 8·5; I, 24·7; 0·46 D), and ***deuterated*** **16 : 22-*epoxy*-3ξ-*iodo*-26-*methoxycholestane***, m. p. 125—130° (from acetone), $[\alpha]_D$ +6° (*c* 0·39%) (Found: C, 61·7; " H ", 9·1; I, 23·4; MeO, 6·4; 0·98 D. $C_{28}H_{46}DO_2I$ requires C, 61·9; " H ", 8·7; I, 23·3; MeO, 5·7%).

Conversion of Deuterated Tigogenin into **16 : 22-*Epoxy*-3ξ-*iodocholest*-25-*ene*** via pseudo-*Tigogenin*.—Deuterated tigogenin (1·56 D), prepared from tigogenin acetate as described above, was converted by the method described previously into deuterated *pseudo*tigogenin (0·6 D). The crude product was dissolved in methanol (100 ml.), concentrated hydrochloric acid (10 ml.) was added, and the solution boiled for 45 min., then poured into water. The solid was collected, washed, dried, chromatographed on neutral alumina, and crystallised from methanol to give deuterated tigogenin, m. p. 200—203°, $[\alpha]_D$ −63° (*c* 0·75%) (Found: C, 77·9; " H ", 10·6;

0·48 D), $\nu_{max.}$ 2120 (w), 920, 896, 885 cm.$^{-1}$. This was converted into deuterated dihydrotigogenin, m. p. 169—171°, $[\alpha]_D$ −4° (*c* 0·76%) (Found: C, 77·8; "H", 11·0; 0·49 D). The ditoluene-*p*-sulphonate (0·48 D) was converted into deuterated 16 : 22-epoxy-3ξ : 26-di-iodocholestane, m. p. 141—146°, $[\alpha]_D$ +4·5° (*c* 0·73%) (Found: C, 51·2; "H", 6·6; I, 39·5; 0·47 D). Dehydroiodination gave 16 : 22-epoxy-3ξ-iodocholest-25-ene, m. p. 93—95°, $[\alpha]_D$ +7° (*c* 0·83%) (Found: C, 63·6; H, 8·2; I, 24·8; no deuterium), and deuterated 16 : 22-epoxy-3ξ-iodo-26-methoxycholestane, m. p. 124—129°, $[\alpha]_D$ +7° (*c* 0·54%) (Found: C, 62·5; "H", 8·7; I, 22·4; MeO, 7·0; 0·55 D).

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544. *Chemical Applications of Nuclear Quadrupole Resonance Spectroscopy. Part I. Some Chloro-derivatives of Nitrogen Heterocycles.*

By M. J. S. Dewar and E. A. C. Lucken.

Nuclear quadrupole resonance spectra of a number of chloro-derivatives of pyridine, pyrimidine, 1 : 3 : 5-triazine, and quinoline have been measured with a frequency-modulated externally quenched, super-regenerative spectrometer. The observed frequencies indicate appreciable π-bonding between chlorine and the ring, more than in the isoconjugate benzene and naphthalene derivatives. Inductive effects are also important, but appear to be mainly of short range, transmitted through the σ-bonds. The theoretical implications are discussed.

Nuclear quadrupole resonance spectroscopy provides a novel and promising method for investigating the electron distributions in molecules. Radio-frequency absorption due to nuclear quadrupole resonance transitions was first observed in 1950 by Dehmelt and Kruger [1] and a number of papers have since been published on this field. Such transitions are possible whenever a nucleus of spin at least unity is surrounded by an electron cloud which is not completely symmetrical. In this case the nucleus must orient itself relatively to the electron cloud in one of $(2I + 1)$ ways, where the spin of the nucleus is I. If $I > \frac{1}{2}$, the nucleus will not in general be spherically symmetrical, but will possess a quadrupole moment; the electrostatic interaction between the unsymmetrical nucleus and the unsymmetrical electron cloud will depend on their mutual orientation, and so the various orientational states have different energies. Transitions between them can, as usual, be induced by electromagnetic radiation, but the frequencies are so low that they lie in the radio region, usually in the range 1—1000 Mc./sec. The energy differences are functions of the quadrupole moment of the nucleus and the asymmetry of the electron distribution; the transition frequencies for a given nucleus in different molecules are therefore a measure of the electronic asymmetry, and it can be shown that the only significant contribution to this arises from the *p*-electrons present.[2] Consequently measurements of nuclear quadrupole resonance frequencies provide information concerning the distribution of *p*-electrons in molecules—information which cannot be obtained directly in any other way and is of great interest in the case of conjugated systems in organic molecules. The mathematical theory has been well reported by Ramsey.[3]

[1] Dehmelt and Kruger, *Naturwiss.*, 1951, **37**, 111.
[2] Townes and Dailey, *J. Chem. Phys.*, 1949, **17**, 782.
[3] Ramsey, "Nuclear Moments," Wiley, New York, 1954.

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Measurements of this kind have been used mainly to study inductive effects and hybridisation in σ-bonds. The number of " organic " atoms that possess spins of unity or greater is unfortunately limited, and most of the work has been confined to halogen derivatives. Halide ions are spherically symmetrical and show no nuclear quadrupole resonance transitions; in covalent compounds RX, the halogen has effectively seven valency electrons (six unshared electrons and a half share in the pair forming the bond), one less than in the ion X^-. The resulting asymmetry gives rise to nuclear quadruple resonance transitions. If the bond R ⟶ X is polar, as indicated, X will have effectively more than seven valency electrons; the electronic asymmetry is then less, and so the nuclear quadrupole resonance frequency is also lowered. For a variety of alkyl chlorides, for example, the frequencies of chlorine run parallel [4] to the expected inductive effect of the alkyl group.

One application of this idea concerns the chlorine and bromine frequencies in substituted chloro- and bromo-benzenes. In each case the nuclear quadrupole resonance frequency follows the Hammett relation.[5] This would be expected, since the Hammett σ-constant provides a measure of the change in inductive effect of phenyl due to substituents. For chlorine, the observed relation is:

$$f = 1{\cdot}0248\sigma + 34{\cdot}826\ (\pm 0{\cdot}36) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where f is the observed nuclear quadrupole resonance frequency in Mc./sec.

When the halogen is attached to an unsaturated system, π-bonding is possible between halogen and the adjacent carbon atom. Moderate π-bonding can be shown to lower the nuclear quadrupole resonance frequency; this accounts for the fact that the chlorine frequencies in chlorobenzene [5] (34·6 at 76° K) and vinyl chloride [6] (33·6 at 20° K) are similar to those in alkyl chlorides (31—34 Mc./sec. at 96° K) although the sp^2-carbon atoms in the former are much more electronegative than the sp^3-carbon atoms in the latter.

Measurements of nuclear quadrupole resonance frequencies therefore provide a method for studying the distribution of π-electrons in conjugated systems. This paper is the first of a series describing investigations of this kind. In it we report preliminary work on a number of chloro-derivatives of nitrogen-containing heterocycles.

Experimental

Materials.—2-Chloropyridine was distilled before use, and 2- and 6-chloroquinoline were prepared by standard methods.[7] Cyanuric chloride and 2-chlorolepidine were commercial specimens used without purification. A sample of 7-chloroquinoline was lent by May and Baker Ltd. and the pyrimidine derivatives by Imperial Chemical Industries Limited; we gratefully acknowledge their assistance.

Measurements.—The resonances were detected at temperatures ranging from 86° K to room temperature with a frequency-modulated, externally quenched, super-regenerative spectrometer similar to that of Dean,[8] and the spectra were displayed on an oscilloscope whose time-base was locked to the modulation frequency. Resonance frequencies were measured with a war-surplus frequency meter, type BC221, the side bands being distinguished from the fundamentals by carrying out the measurements at two different quench frequencies. The frequencies are thought to be accurate to ±0·001 Mc./sec. Details of the spectrometer and associated equipment are given in a thesis by one of us.[9]

Results.—The observed frequencies are tabulated.

[4] Livingstone, *J. Phys. Chem.* 1953, **57**, 1792.
[5] Bray and Barnes, *J. Chem. Phys.*, 1957, **27**, 551.
[6] Goldstein and Bragg, *Phys. Rev.*, 1949, **75**, 1943.
[7] Robinson and Perkin, *J.*, 1913, 1977; Fourneau, Trefoud, and Wancolle, *Bull. Soc. chim. France*, 1930, **47**, 738.
[8] Dean, Thesis, Harvard, 1952.
[9] Lucken, Thesis, London, 1958.

Nuclear quadrupole resonance frequencies.

Compound	Frequency (Mc./sec.) at 86° K	195° K	276° K	Room temp.
2-Chloropyridine	34·173	—	—	—
2-Chloroquinoline	33·287	33·102	32·939	32·874 (297°)
6-Chloroquinoline	34·600	34·334	34·132	34·057 (297°)
7-Chloroquinoline	34·681	—	—	—
2-Chlorolepidine	33·655	—	—	33·258 (296°)
2 : 4-Dichloro-3-methylquinoline	34·268 35·627	—	—	33·829 (292°) 34·902
4 : 6-Dichloro-2-methylpyrimidine	35·156	34·949	—	34·695 (294°)
5-Benzyl-4 : 6-dichloro-2-methylpyrimidine	35·015	—	—	34·598 (293°)
4 : 6-Dichloro-2-methyl-5-phenylpyrimidine	35·248	—	—	—
6-Amino-2 : 4-dichloro-5-ethylpyrimidine	34·879 35·044	—	—	34·260 (292°) 34·488
2 : 4 : 6-Trichloropyrimidine	A series of strong closely spaced lines in the region 30—40 Mc./sec. at 86° K.			
Cyanuric chloride	36·724 36·752	36·537	36·346 36·360	36·300 36·316

Discussion

Segel, Barnes, and Bray [10] have reported nuclear quadruple resonance frequencies for the first three compounds in the Table, our values agreeing well with theirs (2-chloropyridine **34·194**, 2-chloroquinoline **33·271**, 6-chloroquinoline **34·628** Mc./sec. at 76° K). Our values for cyanuric chloride also agree well with those reported by Negita and Satou [11] (**36·323**, **36·338** Mc./sec. at 285° K).

For cyanuric chloride the relative intensities of the lines in the doublet vary with temperature. At high temperatures the higher-frequency line is the weaker, at 84° it is the stronger. Our results suggest that this is due to a difference in variation of frequency with temperature, the lines coinciding near 195° K.

The most striking features of the Table are the low frequencies observed for 2-chloropyridine and 2-chloroquinoline. That for 2-chloropyridine is much less than that (**34·6** Mc./sec. at 77° K) reported [6] for chlorobenzene, although the inductive effect of the nitrogen might have been expected to raise the frequency. The difference is too large to be ascribed to the effects of stray fields in the crystal, so one must conclude that the C–Cl bond in chloropyridine has a larger π-order than that in chlorobenzene.

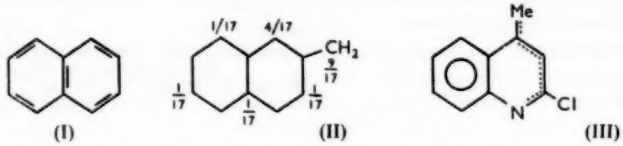
The case of 2-chloroquinoline is probably still more striking, but unfortunately the frequency for 2-chloronaphthalene is not yet known. We tried to obtain a spectrum for this substance but could observe no absorption. However, one can use the observed dissociation constants of 2-naphthylamine ($pK_b = 4{\cdot}11$ at 25° C) or 2-naphthoic acid ($pK_a = 4{\cdot}17$ at 25° C) to calculate an effective σ-constant for the β-naphthyl group; the values so found (0·17 and 0·00 respectively) in conjunction with equation (1) lead to a predicted value **34·9** ± 0·4 Mc./sec. for 2-chloronaphthalene. The difference (**1·6** Mc./sec.) between this and the value observed for 2-chloroquinoline is much greater than the difference between chlorobenzene and 2-chloropyridine.

The explanation of these differences in terms of π-bonding seems quite reasonable. Measurements of the microwave spectrum of vinyl chloride [12] and of the Zeeman splitting of the nuclear quadrupole resonance spectrum of *p*-dichlorobenzene [13] show that the C–Cl bond in such compounds has a double-bond character of 5—15%. Since the π-bond between chlorine and the ring is a dative π-bond, and since the corresponding charge displacement should be easier in the case of the more electrophilic heterocyclic systems, one would expect the C–Cl π-bond orders to be greater in the 2-chloro-heterocycles.

The difference in nuclear quadrupole resonance frequency between 2-chloroquinoline

[10] Segel, Barnes, and Bray, *J. Chem. Phys.*, 1956, **25**, 1286.
[11] Negita and Satou, *ibid.*, 1957, **27**, 602.
[12] Goldstein and Bragg, *Phys. Rev.*, 1950, **78**, 347.
[13] Dean, *ibid.*, 1954, **96**, 1053.

(33·287 Mc./sec.) and 2-chloropyridine (34·173 Mc./sec.) implies that the C–Cl bond order is greater in the former compound. It is true that the β-naphthyl group has a somewhat greater conjugative power than the phenyl group,[14] but the disparity seems too small to account for the large difference (0·886 Mc./sec.). We believe that the difference is due to partial bond-fixation in quinoline. Both theoretical calculation and experiment suggest that naphthalene approximates to the classical structure (I); and the same should be true of quinoline. In that case the conjugative interaction between nitrogen and chlorine in 2-chloroquinoline should be larger than in 2-chloropyridine, since the N=C π-bond order will be larger in the former. Consequently the C–Cl π-bond order should be greater, and the nuclear quadrupole resonance frequency of chlorine less, in 2-chloroquinoline.



(I) (II) (III)

This argument implies that the chlorine frequency should be still less in imidoyl chlorides, where the N=C π-bond order is nearly unity; we are investigating this. It is noteworthy in this connection that the chlorine frequencies for acid chlorides[15] (*e.g.*, sebacoyl chloride 29·118; adipoyl chloride 29·978 Mc./sec.) are very much lower than for vinyl chloride[7] (33·6 Mc./sec.), although the carbonyl-oxygen atom must exert a very large inductive effect. Clearly the conjugation in acid chlorides must be strong, as it should be, if our argument is correct.

The chlorine frequencies in 6- and 7-chloroquinoline are very close to the value predicted for 2-chloronaphthalene; this is in accord with the values of the Hammett σ-function for the 6- and the 7-quinolyl group (0·23, 0·24 respectively[16]) which are similar to the value for 2-naphthyl. The effect of nitrogen does not seem to be transmitted to the 6- or 7-position.

One can assess the effect of the nitrogen atom by an approximate method derived by Longuet-Higgins.[17] The chloroquinolines are isoconjugate with the 2-naphthylmethyl anion, in which the formal charge is distributed approximately as in (II). Since the charge is much greater in the 1-position than in the 5- or the 8-position, nitrogen should have a much greater effect in the 1-position (as in 2-chloroquinoline) than in the 5- or 8-position (as in 6- or 7-chloroquinoline). The actual difference will be still greater, for the values in (II) are calculated on the assumption that the C–C bonds are identical; the fixation of bonds in quinoline [cf. (I)] will accentuate the difference between the 1-position and the others.

Any difference in conjugation between 6- and 7-chloroquinoline should, according to (II), make the nuclear quadrupole resonance frequency smaller for the 7-isomer; in fact it is somewhat greater. However, this argument neglects the inductive effect of nitrogen. In the first place this will raise both frequencies by an inductive effect operating through the intervening σ-bonds; and the effect should be more than twice as great[14] in the 7-position as in the 6-position which is one atom further removed from nitrogen. In the second place, the inductive effect will raise the electronegativities of the atoms adjacent to nitrogen and make them behave qualitatively like heteroatoms; when allowance is made for this, the conjugative influence of nitrogen on the 6- and the 7-position is predicted to be much the same.[18]

The frequencies for chlorine in the pyrimidine derivatives are much higher than for

[14] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3361.
[15] Bray, *J. Chem. Phys.*, 1955, **23**, 703.
[16] Elderfield and Siegel, *J. Amer. Chem. Soc.*, 1951, **73**, 5622.
[17] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265, 275, 283.
[18] Brown and Dewar, *J.*, 1953, 2406.

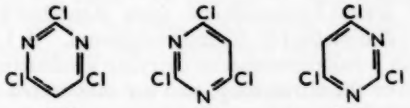
2-chloropyridine; evidently the inductive effects of the extra nitrogen and chlorine atoms outweigh any increase in conjugation due to the extra nitrogen atom. The same is true for cyanuric chloride, the chlorine frequencies being much higher than those for any of the pyrimidine derivatives. A comparison of the frequencies for 4 : 6-dichloro-2-methylpyrimidine with those for its 5-phenyl and 5-benzyl derivative indicates that phenyl exerts a small $+I$ effect, benzyl a small $-I$ effect, as current theory and the values of the corresponding σ-constants [19] suggest.

It is therefore surprising that the nuclear quadrupole resonance frequency for 2-chlorolepidine (33·655 Mc./sec.) is greater than for 2-chloroquinoline (33·287 Mc./sec.). We think this can be ascribed to mutual conjugation between the methyl group and the nitrogen atom, which tends to even out the bond orders in the nitrogen-containing ring, as indicated in (III), and so lower the order of the 1 : 2-bond. If we are correct in assuming that the very low chlorine frequency in 2-chloroquinoline is due to a high 1 : 2-bond order, any decrease in the order of this bond should raise the nuclear quadrupole resonance frequency.

Further evidence for the bond fixation is provided by 2 : 4-dichloro-3-methylquinoline, where the two chlorine frequencies presumably correspond to the two dissimilar chlorine atoms. The inductive effects of the 3-methyl group and the 4-chloro-atom on the 2-chlorine atom can be estimated from the results for the pyrimidines. For 5-benzyl-4 : 6-dichloro-2-methylpyrimidine, the effect of the distant methyl group and the 1-nitrogen atom on the 4-chlorine atom must be small. The main inductive effects arise from the 3-nitrogen atom, the 5-benzyl group, and the 6-chlorine atom. The difference in total inductive effect between the pyrimidine and 2-chloropyridine is then essentially that of an *o*-alkyl group and a *m*-chlorine atom; the corresponding difference in frequency is 0·842 Mc./sec. The difference between the 2-chlorine frequencies in 2-chloroquinoline and 2 : 4-dichloro-3-methylquinoline should therefore be about 0·85 Mc./sec., since the same inductive grouping is involved. This identifies the line at 34·268 Mc./sec. with the 2-chlorine atom (difference from 2-chloroquinoline, 0·895 Mc./sec.), and the line at 35·627 Mc./sec. with the 4-chlorine atom (difference from 2-chloroquinoline, 2·340 Mc./sec.). Now if the difference between the two chlorine frequencies were due to inductive effects, one would expect the 4-chlorine atom to have the lower frequency, for the 2-chlorine is nearer to the nitrogen. If all the bonds in the ring were similar, one would expect the conjugative effect to be greater in the 4-position, and this would also lead to a lower frequency for the 4-chlorine atom. In fact the frequency for the 4-chlorine is very much the higher. The only reasonable explanation seems to be that partial bond-fixation in quinoline [cf. (I)] isolates the 4-chlorine atom from the nitrogen atom; the C–Cl π-bond order is therefore greater, and the frequency consequently less, for the 2-chlorine atom.

Unfortunately no physical data (structure determinations or C–Cl bond stretching frequencies) have been reported which would enable one to deduce the relative C–Cl bond orders in 2- and 4-chloroquinoline. However the much greater chemical reactivity of chlorine in the 4-isomer may be partly due to a lower C–Cl bond order and consequent lower conjugation energy.

The spectrum of 2 : 4 : 6-trichloropyrimidine, unlike those of the isoconjugate 1 : 3 : 5-trichlorobenzene or cyanuric chloride, contains a multitude of lines covering a wide frequency range. This can probably be attributed to the asymmetry of the pyrimidine



(IV) (V) (VI)

derivative. The orientations (IV), (V), (VI) are not identical for the solid state, but differ very little in geometry. We think it likely that the molecules are in consequence packed

[19] Jaffe, *Chem. Rev.*, 1953.

randomly in the crystal, just like the molecules in crystals of nitric oxide. Each chlorine can therefore find itself in one of a number of possible environments; and each environment gives rise to a different chlorine frequency. We are examining trichloropyrimidine in a spectrometer of a different type, where it should be possible to resolve the individual lines, and we shall also examine 2 : 4 : 6-trichloropyridine, which should show similar behaviour, in the hope of relating the number of observed lines to the structure of the crystal.

We thank the Royal Society and the University of London for grants for the purchase of apparatus, and Imperial Chemical Industries Limited and May and Baker Ltd. for the loan of compounds. One of us (E. A. C. L.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1. [*Received, March 3rd,* 1958.]

545. *Diphenylenes. Part II.* Syntheses of Substituted Diphenylenes and of Related Diphenyls.*

By WILSON BAKER, J. W. BARTON, and J. F. W. MCOMIE.

Unambiguous syntheses of a number of methyl-, methoxy-, nitro-, bromo-, and acetyl-diphenylenes and -diphenyls are described. These compounds were required in order to orientate products, obtained by direct substitution into the diphenylene nucleus, which are described in the following paper. The diphenylenes were all synthesised from the appropriate 2 : 2′-di-iododiphenyls, *e.g.*, (IV), by treatment with cuprous oxide.

FURTHER studies on the chemistry of diphenylene, and in particular investigation of the course of substitution in the nucleus, are described in this and the following paper. Three methods have been used for the orientation of substituents introduced directly into diphenylene: (1) comparison with substituted diphenylenes of known orientation synthesised from appropriately substituted 2 : 2′-di-iododiphenyls; (2) reduction of the substituted diphenylene with Raney nickel in alcohol whereby the four-membered ring is opened, giving substituted diphenyls whose orientation is established by comparison with diphenyls of known orientation synthesised by more direct methods; (3) conversion of an already orientated derivative into a substance prepared by direct substitution into the nucleus, or *vice versa*.

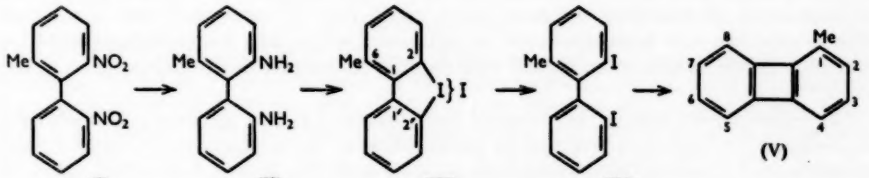
This paper describes the synthesis of a number of mono- and di-substituted diphenylenes and of a few diphenyl derivatives, most of which were required in order to establish the orientation of products, described in the following paper, obtained as the result of direct substitution in the diphenylene nucleus.

Apart from some minor modifications and one exception (2-bromodiphenylene) the diphenylenes have been prepared by the following general method, illustrated by the synthesis of 1-methyldiphenylene. An Ullmann reaction between one molecule each of *o*-iodonitrobenzene and 2-iodo-3-nitrotoluene gave 2-methyl-6 : 2′-dinitrodiphenyl (I) accompanied by some 2 : 2′-dimethyl-6 : 6′-dinitrodiphenyl. A 1-substituted diphenylene ultimately results from an *o*-iodonitrobenzene carrying a substituent in the *ortho*-position to either the iodine atom or the nitro-group, and a 2-substituted diphenylene results from the use of an *o*-iodonitrobenzene with a substituent in the *para*-position either to the

* The paper entitled " Preparation and Reactions of Diphenylene " by W. Baker, M. P. V. Boarland, and J. F. W. McOmie [1] is to be regarded as Part I of this series.

[1] Baker, Boarland, and McOmie, *J.*, 1954, 1476.

iodine atom or to the nitro-group; in each case the more accessible starting material was chosen. Reduction of the dinitrodiphenyl (I) to the diamine (II) followed by tetrazotisation and treatment with potassium iodide gave a mixture of 6-methyldiphenylene-2 : 2′-iodonium iodide (III) and the isomeric 2 : 2′-di-iodo-6-methyldiphenyl (IV). These two di-iodo-, and similarly related, compounds may be separated by taking advantage of the



much smaller solubility in organic solvents of the ionised compound. In practice, however, this is not necessary because in the final step in the synthesis, involving rapid heating at 350° with cuprous oxide, the iodonium iodide (III) is first converted into the di-iodo-compound (IV) from which the iodine atoms are lost to give 1-methyldiphenylene (V). This method of cyclisation to a diphenylene, originally due to Lothrop,[2] with the improvements described by Baker, Boarland, and McOmie,[1] remains the most practical for their preparation. Other methods by which the diphenylene nucleus has been prepared are discussed in a forthcoming comprehensive article by Baker and McOmie.[3]

1-*Methyldiphenylene* (V).—This was prepared as described. It is a liquid at room temperature and was characterised as its picrate and as its complex with 2 : 4 : 7-trinitrofluorenone. It may be recalled that 1-methylnaphthalene, unlike 2-methylnaphthalene, is also a liquid at room temperature.

2-*Methyldiphenylene*.—This solid was prepared from *o*-iodonitrobenzene and 4-iodo-3-nitrotoluene, as in the case of its isomeride. It was purified by regeneration from its picrate, and was characterised as its complex with 2 : 4 : 7-trinitrofluorenone.

1-*Methoxydiphenylene*.—The starting point for this synthesis was 2-iodo-3-nitroanisole, m. p. 102·5—103·5°, which was prepared by methylation of 2-iodo-3-nitrophenol, itself obtained from *m*-nitrophenol by acetoxymercuration followed by treatment with iodine.[4] The substance, m. p. 122—123°, obtained from *m*-nitrophenol by direct iodination and methylation [5,6] has been shown [7] not to be 2-iodo-3-nitroanisole. A mixed Ullmann reaction between *o*-iodonitrobenzene and 2-iodo-3-nitroanisole gave the two symmetrical coupling products and a 12% yield of 2-methoxy-6 : 2′-dinitrodiphenyl. The usual sequence of reactions *via* the diamine and the two di-iodo-compounds then gave 1-methoxydiphenylene, the yield in the final stage being 25%, after isolation as the 2 : 4 : 7-trinitrofluorenone complex.

2-*Methoxy- and* 2-*Hydroxy-diphenylene*.—The crossed Ullmann reaction between *o*-iodonitrobenzene and 4-iodo-3-nitroanisole gave a difficultly separable mixture of the three coupling products. The 4-methoxy-2 : 2′-dinitrodiphenyl was converted as in the previous cases into the related iodonium iodide, but the cyclisation to 2-methoxydiphenylene occurred in only 8% yield. An attempt to demethylate 2-methoxydiphenylene with hydrobromic and acetic acid led only to extensive decomposition, but 2-hydroxydiphenylene was obtained by heating the ether for five minutes with pyridine hydrochloride.

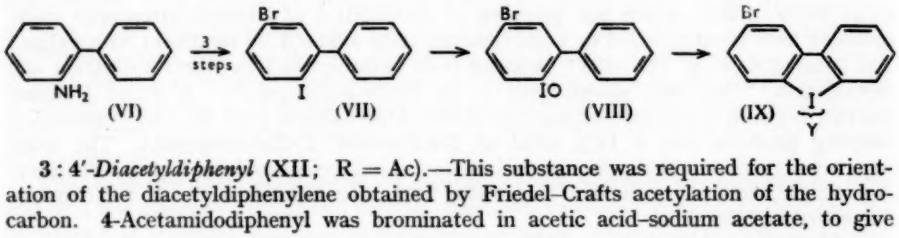
[2] Lothrop, *J. Amer. Chem. Soc.*, 1941, **63**, 1187; 1942, **64**, 1698.
[3] Baker and McOmie, Chapter on "Cyclobutadiene and Related Compounds" in "Non-benzenoid Aromatic Compounds," Ed. D. Ginsburg, Interscience Publ. Inc., New York, 1958.
[4] Wawzonek and Wang, *J. Org. Chem.*, 1951, **16**, 1271.
[5] Schlieper, *Ber.*, 1893, **26**, 2465.
[6] Datta and Prasad, *J. Amer. Chem. Soc.*, 1917, **39**, 441.
[7] Brenans and Larivaille, *Compt. rend.*, 1935, **201**, 81.

1 : 8-*Dimethoxydiphenylene.*—2 : 2′-Dimethoxy-6 : 6′-dinitrodiphenyl, obtained as a by-product in the synthesis of 1-methoxydiphenylene, was converted *via* the related diamino- and di-iodo-compounds into 1 : 8-dimethoxydiphenylene. 2 : 7-Dimethoxydiphenylene has been similarly prepared by Lothrop.[2]

2-*Nitrodiphenylene.*—Wasylewsky, Brown, and Sandin [8] converted diphenylene-2 : 2′-iodonium iodide into the nitrate, which in concentrated sulphuric acid passed into 4-nitrodiphenylene-2 : 2′-iodonium sulphate which could then be converted into the nitrate. This nitrate has now been converted by potassium iodide into 4-nitrodiphenylene-2 : 2′-iodonium iodide, which when heated with cuprous oxide gave 2-nitrodiphenylene in 20% yield.

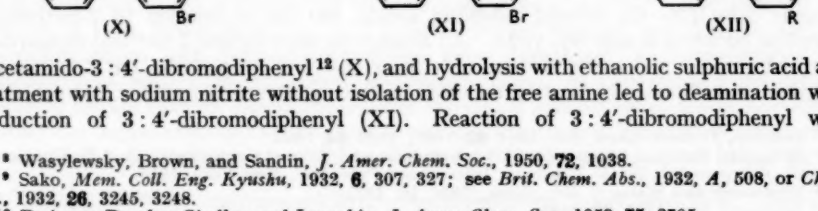
2 : 6-*Dinitrophenylene.*—The essential intermediate for this synthesis, 2 : 2′-diamino-4 : 5′-dinitrodiphenyl, was prepared by modification of the method due to Sako,[9] namely, nitration of 2 : 2′-disuccinimidodiphenyl, separation of the desired 4 : 5′- from the 4 : 4′- and 5 : 5′-dinitro-derivatives, and hydrolysis with ethanolic hydrochloric acid. Subsequent conversion into 2 : 6-dinitrodiphenylene was carried out in the usual way, but the yield in the final step was not above 1%.

2-*Bromodiphenylene.*—The 5-bromodiphenylene-2 : 2′-iodonium iodide (IX; Y = I) required for this synthesis was prepared from the commercially available 2-aminodiphenyl (VI), which was brominated directly to 2-amino-5-bromodiphenyl, then diazotised and treated with potassium iodide giving 5-bromo-2-iododiphenyl (VII). Oxidation of this with peracetic acid gave 5-bromo-2-iodosodiphenyl (VIII). It was shown by Beringer *et al.*[10] that iodosobenzenes condense with aromatic compounds in presence of sulphuric acid to give diaryliodonium salts, and Collette, McGreer, Crawford, Chubb, and Sandin [11] have applied this reaction to 2-iodosodiphenyl, thereby converting it in very high yield into a diphenylene-2 : 2′-iodonium salt. Taking advantage of this reaction 5-bromo-2-iodosodiphenyl (VIII) has been converted in high yield into 5-bromodiphenylene-2 : 2′-iodonium hydrogen sulphate (IX; Y = HSO_4), which without isolation gave the related iodide when treated with concentrated aqueous potassium iodide. Final heating with cuprous oxide gave 2-bromodiphenylene in 10% yield, accompanied rather unexpectedly by diphenylene itself in 12% yield.



(VI) (VII) (VIII) (IX)

3 : 4′-*Diacetyldiphenyl* (XII; R = Ac).—This substance was required for the orientation of the diacetyldiphenylene obtained by Friedel–Crafts acetylation of the hydrocarbon. 4-Acetamidodiphenyl was brominated in acetic acid–sodium acetate, to give



(X) (XI) (XII)

4-acetamido-3 : 4′-dibromodiphenyl [12] (X), and hydrolysis with ethanolic sulphuric acid and treatment with sodium nitrite without isolation of the free amine led to deamination with production of 3 : 4′-dibromodiphenyl (XI). Reaction of 3 : 4′-dibromodiphenyl with

[8] Wasylewsky, Brown, and Sandin, *J. Amer. Chem. Soc.*, 1950, **72**, 1038.
[9] Sako, *Mem. Coll. Eng. Kyushu*, 1932, **6**, 307, 327; see *Brit. Chem. Abs.*, 1932, *A*, 508, or *Chem. Abs.*, 1932, **26**, 3245, 3248.
[10] Beringer, Drexler, Gindler, and Lumpkin, *J. Amer. Chem. Soc.*, 1953, **75**, 2705.
[11] Collette, McGreer, Crawford, Chubb, and Sandin, *ibid.*, 1956, **78**, 3819.
[12] Case and Sloviter, *ibid.*, 1937, **59**, 2381.

cuprous cyanide in pyridine gave a 67% yield of 3 : 4′-dicyanodiphenyl (XII; R = CN), which was converted by treatment with an excess of methylmagnesium iodide into 3 : 4′-diacetyldiphenyl (XII; R = Ac).

The ultraviolet absorption spectra of some of the compounds described in this paper are recorded in Part III.

Experimental

2-Methyl-6 : 2′-dinitrodiphenyl (I).—2-Amino-3-nitrotoluene [13] was converted into 2-iodo-3-nitrotoluene,[14] and to a stirred mixture of this iodo-compound (15 g.), *o*-iodonitrobenzene (14·5 g.), and nitrobenzene (30 ml.) in an oil-bath at 190—200° was added copper bronze (15 g.) during ½ hr. After a further ½ hour's heating benzene was added, the mixture was filtered and steam-distilled, and the non-volatile oil was collected into ether and distilled, mainly at 175—180°/0·3 mm. The product crystallised on slow evaporation at room temperature of its solution in methanol. Two further recrystallisations gave *2-methyl-6 : 2′-dinitrodiphenyl* as pale yellow needles (3·8 g.), m. p. 70—71° (Found: C, 60·8; H, 4·0; N, 10·7. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·9%). The mother-liquor yielded 2 : 2′-dimethyl-6 : 6′-dinitrodiphenyl, m. p. 106—107° (lit.,[3] m. p. 107—108°).

2 : 2′-Diamino-6-methyldiphenyl (II).—The preceding dinitro-compound (4 g.) in ethanol (75 ml.) was reduced by hydrogen at 3 atm. in presence of platinum oxide (0·1 g.) (4 hr.). The filtered, and then concentrated solution was diluted with water, and the solid recrystallised from 50% ethanol, giving *2 : 2′-diamino-6-methyldiphenyl* (2·8 g.) as a hemihydrate, m. p. 61—62° (Found: C, 75·4; H, 6·8; N, 13·7. $C_{13}H_{14}N_2,\frac{1}{2}H_2O$ requires C, 75·4; H, 7·2; N, 13·5%). In a desiccator the substance loses water and liquefies.

2 : 2′-Di-iodo-6-methyldiphenyl (IV) *and 6-Methyldiphenylene-2 : 2′-iodonium Iodide* (III).—The preceding diamine (2·8 g.) in concentrated hydrochloric acid (15 ml.) and water (15 ml.) was tetrazotised at 0° by slow addition of sodium nitrite (2·1 g.) in water (10 ml.), and a concentrated aqueous solution of potassium iodide (9 g.) was then added. After 1 hr. the mixture was warmed on the water-bath and treated with excess of sodium hydrogen sulphite, and the solid was collected, washed, and warmed with methanol (100 ml.), leaving a brown residue (1·1 g.) of crude 6-methyldiphenylene-2 : 2′-iodonium iodide. The methanolic extract deposited 2 : 2′-di-iodo-6-methyldiphenyl which after several crystallisations was obtained as an orange-brown solid (1·5 g.), m. p. 96—97° (Found: C, 37·3; H, 2·3. $C_{13}H_{10}O_2$ requires C, 37·2; H, 2·4%).

1-Methyldiphenylene (V).—When either of the above di-iodo-derivatives (1·3 g.) was finely powdered with cuprous oxide (20 g.) and rapidly heated in a metal-bath at 350° for 5 min. as previously described [1] a yellow oil was obtained. This was distilled in steam, and the oil was collected into ether and treated with ethanolic picric acid, giving the scarlet *picrate* (0·5 g.) of 1-methyldiphenylene, which after recrystallisation from ethanol had m. p. 91—92° (Found: C, 57·8; H, 3·7; N, 10·8. $C_{13}H_{10},C_6H_3O_7N_3$ requires C, 57·8; H, 4·0; N, 10·6%). *1-Methyldiphenylene*, regenerated from the picrate by passage of its solution in benzene through an alumina column, forms a yellow oil (Found: C, 93·8; H, 5·9. $C_{13}H_{10}$ requires C, 94·0; H, 6·0%). The 2 : 4 : 7-*trinitrofluorenone complex* separates from ethanol–ethyl acetate in deep scarlet needles, m. p. 162—163·5° (Found: C, 64·6; H, 3·3; N, 8·9. $C_{13}H_{10},C_{13}H_5O_7N_3$ requires C, 64·8; H, 3·1; N, 8·7%).

4-Methyl-2 : 2′-dinitrodiphenyl.—*o*-Iodonitrobenzene (14·5 g.) and 4-iodo-3-nitrotoluene (15 g.) (prepared from the corresponding amines by Wheeler and Liddle's method [14]) in nitrobenzene (30 ml.) were stirred at 170—180°, and copper bronze (15 g.) added during ½ hr. After being heated for a further ½ hr. the mixture was cooled, filtered after the addition of benzene, and steam-distilled, and the residue which solidified was crystallised from ethanol, giving *4-methyl-2 : 2′-dinitrodiphenyl* as pale yellow needles, m. p. 93—95° (7·3 g., 54%). Sublimation at 150—160°/2 mm. and recrystallisation gave material of m. p. 94—95° (Found: C, 60·7; H, 3·7; N, 10·6. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·6%).

2 : 2′-Diamino-4-methyldiphenyl.—The preceding dinitro-compound (7 g.) was hydrogenated at 110°/6—7 atm. for 2 hr. in ethanol (75 ml.) in presence of Raney nickel (1 g.); heating was

[13] Cohen, *J.*, 1891, **79**, 1127.
[14] Wheeler and Liddle, *Amer. Chem. J.*, 1909, **42**, 451.

XUM

then stopped and reduction continued for 2 hr. The filtered solution was distilled, giving 2 : 2′-*diamino*-4-*methyldiphenyl*, b. p. 160—164°/0·8 mm. (3·1 g., 59%) (Found: C, 78·6; H, 7·1; N, 14·6. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1; N, 14·2%).

4-*Methyldiphenylene*-2 : 2′-*iodonium Iodide and* 2 : 2′-*Di-iodo*-4-*methyldiphenyl*.—The preceding diamine (2·8 g.) was tetrazotised and treated with potassium iodide as described in the case of its isomer, and the crude, washed product was extracted with methanol (100 ml.) in a Soxhlet apparatus. There remained in the thimble the iodonium iodide as a cream-coloured powder, m. p. 201—202° (decomp.) (2·1 g.). The product from the extract was sublimed at 100—110°/1 mm. and crystallised twice from methanol, giving 2 : 2′-*di-iodo*-4-*methyldiphenyl* as prisms, m. p. 85—86° (0·8 g.) (Found: C, 36·7; H, 2·2. $C_{14}H_{10}I_2$ requires C, 37·2; H, 2·4%).

2-*Methyldiphenylene*.—After either of the above di-iodo-compounds had been heated at 350—370° with 10 times the weight of dry cuprous oxide as described previously,[1] the product, a resinous solid, was steam-distilled, giving a yellow solid in low yield. Crystallisation from saturated ethanolic picric acid gave a picrate as crimson needles, m. p. 86—87° after recrystallisation. The *hydrocarbon* was regenerated by passing the picrate in ethanol through alumina and after sublimation at 60—80°/10 mm. and crystallisation from methanol formed pale straw-coloured needles, m. p. 45—46° (Found: C, 93·7; H, 6·0. $C_{13}H_{10}$ requires C, 94·0; H, 6·0%). The 2 : 4 : 7-*trinitrofluorenone complex* prepared in and crystallised from acetic acid formed deep purple needles, m. p. 150—151° (Found: C, 64·7; H, 3·2; N, 8·9. $C_{26}H_{15}O_7N_3$ requires C, 64·8; H, 3·1; N, 8·7%).

2-*Iodo*-3-*nitroanisole*.—2-Iodo-3-nitrophenol[4] (35 g.) was methylated in 10% aqueous sodium hydroxide (50 ml.) at 60° by shaking it with methyl sulphate (35 ml.) and more alkali (50 ml.) in alternate portions; finally the mixture was refluxed for 2 hr. with 20% aqueous sodium hydroxide (50 ml.), cooled, and the washed solid crystallised from carbon tetrachloride, giving bright yellow plates, m. p. 97—100° (22·5 g.). After several crystallisations the m. p. was 102·5—103·5° (Found: C, 30·0; H, 2·4; N, 5·3; I, 45·3. $C_7H_6O_3NI$ requires C, 30·1; H, 2·2; N, 5·0; I, 45·5%).

2-*Methoxy*-6 : 2′-*dinitrodiphenyl*.—*o*-Iodonitrobenzene (23 g.) and 2-iodo-3-nitroanisole (21·5 g.) were stirred and heated in nitrobenzene (40 ml.) at 190—200° for 50 min., copper bronze (25 g.) being added during the first 20 min. The mixture was diluted with benzene, filtered, and steam-distilled, the residue was dissolved in hot acetone (charcoal), then concentrated, and warm methanol was added. On cooling, 2 : 2′-dimethoxy-6 : 6′-dinitrodiphenyl (3·8 g.) separated. The product from the mother-liquor was fractionally crystallised from methanol, giving 2-*methoxy*-6 : 2′-*dinitrodiphenyl* (2·6 g., 12%), m. p. 152—154·5°, and crude 2 : 2′-dinitrodiphenyl (2·3 g.). After further crystallisation from methanol and sublimation under reduced pressure the pure 2-methoxy-6 : 2′-dinitrodiphenyl had m. p. 157—158° (Found: C, 56·9; H, 3·7; N, 10·2. $C_{13}H_{10}O_5N_2$ requires C, 57·0; H, 3·7; N, 10·2%).

A closely similar reaction using *o*-bromonitrobenzene and 2-chloro-3-nitroanisole but without solvent gave a 10% yield of 2-methoxy-6 : 2′-dinitrodiphenyl.

2 : 2′-*Diamino*-6-*methoxydiphenyl*.—The preceding dinitro-compound (4·9 g.), granulated tin (20 g.), concentrated hydrochloric acid (40 ml.), and acetic acid (10 ml.) were heated on a water-bath until a clear solution was obtained. After dilution with water (100 ml.) and passage of hydrogen sulphide, the filtered solution was made alkaline with sodium hydroxide and extracted with ether. The extract yielded 2 : 2′-*diamino*-6-*methoxydiphenyl*, needles (from ethanol), m. p. 98—99° (3·1 g.) (Found: C, 72·7; H, 6·6; N, 12·9. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1%).

6-*Methoxydiphenylene*-2 : 2′-*iodonium Iodide and* 2 : 2′-*Di-iodo*-6-*methoxydiphenyl*.—The 2 : 2′-diamino-6-methoxydiphenyl (2·6 g.) was converted by the procedure described in the case of 2 : 2′-diamino-6-methyldiphenyl (II) into a mixture of 6-methoxydiphenylene-2 : 2′-iodonium iodide, a light grey powder, m. p. 209—210° (decomp.) (1·1 g.), and 2 : 2′-*di-iodo*-6-*methoxydiphenyl* which separated from methanol (charcoal) in golden-yellow needles, m. p. 138·5—139·5° (1·2 g.) (Found: C, 36·1; H, 2·2; OMe, 7·3. $C_{13}H_7I_2$·OMe requires C, 35·8; H, 2·3; OMe, 7·1%).

1-*Methoxydiphenylene*.—A mixture of the preceding di-iodo-compound (0·6 g.), the iodonium iodide (0·9 g.), and cuprous oxide (25 g.) was heated as in the previous diphenylene preparations, and the product steam-distilled, extracted with ether, and treated with 2 : 4 : 7-trinitrofluorenone (0·35 g.) in acetic acid–ethanol. The *complex* (0·43 g.) after recrystallisation formed deep maroon needles, m. p. 157·5—159° (Found: C, 62·5; H, 3·2; N, 8·3. $C_{26}H_{15}O_8N_3$ requires

C, 62·8; H, 3·0; N, 8·5%). Dissociation was effected by passing its benzene solution through alumina, and the product was twice distilled at *ca.* 150°/16 mm. on to a cold-finger condenser, giving 1-*methoxydiphenylene* as pale-yellow needles, m. p. 41—42° (Found: C, 85·4; H, 5·6. $C_{13}H_{10}O$ requires C, 85·7; H, 5·5%).

4-*Methoxy*-2 : 2′-*dinitrodiphenyl*.—*o*-Iodonitrobenzene (100 g.) and 4-iodo-3-nitroanisole (112 g.) in nitrobenzene (200 ml.) were stirred at 190—200° during slow addition of copper bronze (100 g.) and for ½ hr. after. The cooled mixture was diluted with benzene, filtered, and steam-distilled to remove the solvents, and the non-volatile product crystallised from methanol (charcoal). Two crops (total 13 g.) of crude 4 : 4′-dimethoxy-2 : 2′-dinitrodiphenyl, m. p. 122—126°, were obtained, and slow evaporation at room temperature cause the deposition of successive crops of crude 4-*methoxy*-2 : 2′-*dinitrodiphenyl* which was recrystallised from methanol, giving material of m. p. 92—100° (42 g.). Repeated crystallisation from methanol finally gave flat, bright-yellow needles, m. p. 108—109°, which slowly darkened on exposure to light (Found: C, 57·0; H, 3·8; N, 10·1; OMe, 11·7. $C_{12}H_7O_4N_2{\cdot}OMe$ requires C, 57·0; H, 3·7; N, 10·2; OMe, 11·3%).

2-*Methoxydiphenylene*.—The preceding crude dinitro-compound (12·5 g.) was reduced in the manner described for its isomer, giving 2 : 2′-diamino-4-methoxydiphenyl, b. p. 180—185°/0·5 mm. (5·8 g.). Conversion of the diamine (5·5 g.) into 4-methoxydiphenylene-2 : 2′-iodonium iodide (orange-brown powder; 5·1 g.) was carried out as in the case of the preparation of the 6-methyl compound (II); the related 2 : 2′-di-iodo-4-methoxydiphenyl could not be extracted by means of methanol. When the iodonium iodide (14 g.) was heated with cuprous oxide (120 g.), and the product isolated as usual by steam-distillation, crystallisation from light petroleum (b. p. 40—60°) and sublimation at 100—110°/10 mm. gave 2-*methoxydiphenylene* (0·48 g.) as thick lemon-yellow needles, m. p. 69—70° (Found: C, 85·6; H, 5·3. $C_{13}H_{10}O$ requires C, 85·7; H, 5·5%). The 2 : 4 : 7-*trinitrofluorenone complex* prepared in and crystallised from ethanol forms deep purple needles, m. p. 140—141° (Found: C, 63·0; H, 3·1; N, 8·4. $C_{26}H_{15}O_8N_3$ requires C, 62·8; H, 3·0; N, 8·5%).

2-*Hydroxydiphenylene*.—2-Methoxydiphenylene (50 mg.) and pyridine hydrochloride (500 mg.) were placed in an oil-bath at 230° for 5 min., the flask was rapidly cooled, and the dark contents were washed out with 10% aqueous sodium hydroxide. The filtered solution was acidified, and the solid was sublimed twice at 130—140°/14 mm., giving 2-*hydroxydiphenylene* as pale yellow needles (14 mg.), m. p. 140—141° (Found: C, 86·0; H, 4·7. $C_{12}H_8O$ requires C, 85·7; H, 4·8%). The m. p. was not depressed on admixture with the hydroxydiphenylene, m. p. 139—140°, prepared by oxidising diphenylene with lead tetra-acetate.[1]

2 : 2′-*Diamino*-6 : 6′-*dimethoxydiphenyl*.—2 : 2′-Dimethoxy-6 : 6′-dinitrodiphenyl (see preparation of 2-methoxy-6 : 2′-dinitrodiphenyl) (7·5 g.) was reduced with tin and hydrochloric acid in the same manner as the monomethoxy-compounds, giving 2 : 2′-*diamino*-6 : 6′-*dimethoxydiphenyl* (4·7 g.) which separated from dilute ethanol in hexagonal prisms, m. p. 90—91° (Found: C, 63·8; H, 6·8; N, 10·5. $C_{14}H_{16}O_2N_2,H_2O$ requires C, 64·2; H, 6·9; N, 10·7%).

6 : 6′-*Dimethoxydiphenylene*-2 : 2′-*iodonium Iodide and* 2 : 2′-*Di-iodo*-6 : 6′-*dimethoxydiphenyl*.—The preceding diamine (3·3 g.) was tetrazotised and then treated with potassium iodide, and the products were isolated as in the previous cases, giving the iodonium iodide as an orange-brown powder [0·6 g.; m. p. 168° (decomp.)], insoluble in cold ethanol, and 2 : 2′-*di-iodo*-6 : 6′-*dimethoxydiphenyl* as pale orange needles (2·4 g.), m. p. 182—184° (from methanol; charcoal) [Found: C, 36·4; H, 2·7; OMe, 13·0. $C_{12}H_6I_2(OMe)_2$ requires C, 36·1; H, 2·6; OMe, 13·3%].

1 : 8-*Dimethoxydiphenylene*.—Rapid distillation of the foregoing two iodo-compounds with cuprous oxide as in the previous diphenylene preparations, and prolonged steam-distillation gave 1 : 8-*dimethoxydiphenylene* which crystallised from methanol in bright yellow tablets, m. p. 107—108° (Found in material sublimed at 130°/12 mm.: C, 79·0; H, 5·7. $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7%). This m. p. is the same as that of 2 : 7-dimethoxydiphenylene,[2] but a mixed m. p. shows a depression.

4-*Nitrodiphenylene*-2 : 2′-*iodonium Iodide*.—Diphenylene-2 : 2′-iodonium iodide was converted into 4-nitrodiphenylene-2 : 2′-iodonium nitrate according to the method of Wasylewski, Brown, and Sandin;[3] the crude nitrate (4·5 g.) was supended in boiling water (1 l.), a saturated solution of potassium iodide (10 g.) was added, and the mixture was stirred at 100° for 1 hr. The *iodonium iodide* was collected, digested with boiling water, and dried (2·5 g.); it formed a dull yellow powder, m. p. 197—199° (Found: N, 2·9. $C_{12}H_7O_2NI_2$ requires N, 3·1%).

2-*Nitrodiphenylene*.—Distillation of the preceding iodonium iodide with cuprous oxide in the

usual manner gave a partly solid product which was sublimed at 120°/10 mm. and then crystallised from ethanol, giving material (0·18 g.), m. p. 102—104°. Pure *2-nitrodiphenylene*, prepared by steam-distillation and crystallisation from light petroleum (b. p. 40—60°), formed yellow needles, m. p. 107—108° (Found: C, 72·9; H, 3·7; N, 7·0. $C_{12}H_7O_2N$ requires C, 73·1; H, 3·6; N, 7·1%).

2 : 2′-*Diamino*-4 : 5′-*dinitrodiphenyl*.—2 : 2′-Disuccinimidodiphenyl (20 g.) [15,9] was nitrated according to Sako's directions [9] and the washed, dried product was extracted with hot methanol (1 l.) in a Soxhlet apparatus for 6 hr., leaving 4 : 4′-dinitro-2 : 2′-disuccinimidodiphenyl as a white powder, m. p. 295—304°; the cooled, seeded filtrate yielded a small amount of the same compound (total 4·7 g.). The filtrate was concentrated to 200 ml., the solid collected, and the process repeated till no further solid was obtained. By repeated crystallisation of the whole material from methanol containing 5% of acetic acid there was obtained 4 : 5′-dinitro-2 : 2′-disuccinimidodiphenyl as yellow prisms (9·5 g.), m. p. 270—272° (lit., m. p. 271—272°), and 5 : 5′-dinitro-2 : 2′-disuccinimidodiphenyl as a yellow powder (1·1 g.), m. p. 315—317°. The 4 : 5′-dinitro-compound (16 g.) was hydrolysed by boiling it for 5 hr. with concentrated hydrochloric acid (150 ml.), ethanol (150 ml.), and water (75 ml.), the mixture was poured on ice, and the 2 : 2′-diamino-4 : 5′-dinitrodiphenyl collected, washed and dried whereupon it darkened (7·2 g.; m. p. 170—172°) (lit., dimorphic, yellow form, m. p. 143—144°, orange form, m. p. 179—180°.

4 : 5′-*Dinitrodiphenylene*-2 : 2′-*iodonium Iodide and* 2 : 2-*Di-iodo*-4 : 5′-*dinitrodiphenyl*.—The preceding diamine (1·8 g.) was tetrazotised at 0° in concentrated hydrochloric acid (20 ml.) and water (5 ml.) by slow addition of sodium nitrite (0·97 g.), and the solution then added to a stirred solution of potassium iodide (10 g.) in water (20 ml.), heated gently for ½ hr., and set aside with an excess of sodium hydrogen sulphite. The solid was collected, washed, and boiled with ethanol, leaving the insoluble 4 : 5′-*dinitrodiphenylene*-2 : 2′-*iodonium iodide* as a yellow-brown powder [1·6 g.; m. p. 171—172° (decomp.)]. The ethanol extract yielded a product which was successively sublimed (temp. raised to 180°/0·3 mm.), chromatographed in benzene on alumina, and eluted with the same solvent (leaving bright yellow material on the column), and crystallised from ethanol, giving 2 : 2′-*di-iodo*-4 : 5′-*dinitrodiphenyl* as pale yellow, flat prisms (0·8 g.; m. p. 167—168°) (Found: C, 28·7; H, 1·3; N, 5·3. $C_{12}H_6O_4N_2I_2$ requires C, 29·0; H, 1·2; N, 5·45%).

2 : 6-*Dinitrodiphenylene*.—The crude 4 : 5′-dinitrodiphenylene-2 : 2′-iodonium iodide (1·5 g.) was heated with cuprous oxide (25 g.) at 350° in the usual manner, and the sublimate was crystallised three times from ethanol (charcoal), giving 2 : 6-dinitrodiphenylene as deep yellow needles (3 mg.) which sublimed without melting above 260°. A similar experiment using 2 : 2′-di-iodo-4 : 5′-dinitrodiphenyl (0·5 g.) gave almost the same yield of the dinitrodiphenylene. There was insufficient material for analysis, but the characteristic ultraviolet spectrum was identical with that of the dinitro-compound prepared by the nitration of diphenylene as described in the following paper.

5-*Bromo*-2-*iododiphenyl* (VII).—2-Amino-5-bromodiphenyl hydrobromide was prepared in 97% yield by the direct bromination in carbon tetrachloride of commercial 2-aminodiphenyl (VI) according to the directions of Scarborough and Waters [16] who also established the position of the bromine atom. This hydrobromide (13·2 g.) in water (200 ml.) containing concentrated sulphuric acid (4·2 g.) was diazotised at 0—2°, and a strong solution of potassium iodide (24 g.) added below 5°; the mixture was kept overnight, then warmed to 40°. Free iodine was removed by the addition of sodium thiosulphate, the product extracted with ether, and the organic layer washed with aqueous sodium carbonate and water, dried, and distilled, giving 5-*bromo*-2-*iododiphenyl* as a pale yellow oil (11·5 g.), b. p. 180°/15 mm. (Found: C, 40·5; H, 2·4. $C_{12}H_8BrI$ requires C, 40·2; H, 2·2%).

5-*Bromo*-2-*iodosodiphenyl* (VIII) *and* 5-*Bromodiphenylene*-2 : 2′-*iodonium Iodide* (IX; Y = I).—5-Bromo-2-iododiphenyl (VII) (6 g.) in acetic anhydride (25 ml.) was added at 0° to a solution of peracetic acid (30 ml.) (made by slowly adding 30% hydrogen peroxide to 4 times its volume of acetic anhydride at 0°, and keeping the whole at room temperature overnight). The mixture was kept at room temperature for 18 hr. The solution, which then contained the iodoso-compound (VIII), was treated at 0° with concentrated sulphuric acid (6·5 ml.), and after 6 hr. water (120 ml.) was added, and the mixture shaken and extracted with benzene. The aqueous

[15] Dice and Smith, *J. Org. Chem.*, 1949, **14**, 179.
[16] Scarborough and Waters, *J.*, 1927, 89.

layer was treated with aqueous sodium hydrogen sulphite until no iodine was liberated on addition of potassium iodide, and a concentrated solution of potassium iodide was then added till no further precipitation of the iodonium iodide (IX; Y = I) occurred. This product was collected, washed well with water in which it is almost insoluble, and dried at 60° (yield about 2 g.) (decomp. above 250°).

2-Bromodiphenylene.—The foregoing iodonium iodide (4 g.) was heated at 360° for 20 min. in the usual way with cuprous oxide (40 g.). The distillate, collected by dissolving it in hot methanol, was heated at 70—80°/12 mm. for 3 hr., giving a sublimate of pale yellow needles (0·15 g.), m. p. and mixed m. p. with diphenylene 110—111°. The remaining product (0·28 g.) was converted in ethanol–acetic acid (1 : 2) into the 2 : 4 : 7-trinitrofluorenone complex, m. p. 135—136°. Regeneration of the 2-bromodiphenylene by passage through alumina in benzene, recovery, and sublimation at 115—125°/13 mm. gave cream-coloured plates (0·20 g.), m. p. 64—65°, undepressed when mixed with a specimen prepared by either of the methods described in Part III (for analyses see Part III).

3 : 4′-Dicyanodiphenyl (XII; R = CN).—4-Acetamido-3 : 4′-dibromodiphenyl [12] (X) (10 g.) was refluxed for 24 hr. with ethanol (100 ml.) containing concentrated sulphuric acid (10 ml.). Diluted sulphuric acid (50 ml.; 50% v/v) was added and to the boiling mixture a concentrated aqueous solution of sodium nitrite (8 g.) was dropped in during 1 hr. After being boiled for a further ½ hr. the solution was extracted with ether, and the crude 3 : 4′-dibromodiphenyl (XI) distilled as an amber-coloured oil (5·6 g.; b. p. 135—140°/1 mm.). This dibromo-compound (5·6 g.) was next heated under reflux (bath-temp. 180—190°) for 20 hr. with pyridine (10 ml.) and anhydrous cuprous cyanide (3·6 g.), and the solid, cooled product was shaken alternately several times with a mixture of equal volumes of concentrated aqueous ammonia and water, and with benzene. The benzene extracts were washed with dilute aqueous ammonia, then with 4N-hydrochloric acid, and yielded *3 : 4′-dicyanodiphenyl* which separated from benzene–light petroleum (b. p. 60—80°) as a cream-coloured powder, m. p. 129—131° (Found: C, 82·2; H, 4·2; N, 13·5. $C_{14}H_8N_2$ requires C, 82·4; H, 3·9; N, 13·7%).

3 : 4′-Diacetyldiphenyl (XII; R = Ac).—3 : 4′-Dicyanodiphenyl (1 g.) in benzene (25 ml.) was added to the Grignard reagent prepared from methyl iodide (2·8 g.) and magnesium (0·5 g.) in ether (20 ml.), the ether distilled away, and the benzene solution boiled under reflux for 1 hr. Next day the mixture was heated with dilute hydrochloric acid for 1 hr. The benzene layer and extract yielded a product which was sublimed at 130—140°/0·1 mm., and then crystallised from ethanol. The *3 : 4′-diacetyldiphenyl* (0·4 g.) formed colourless needles, m. p. 101—102° (Found: C, 80·5; H, 5·6. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%).

3 : 3′-Diacetyldiphenyl.—3-Nitroacetophenone [17] was reduced to 3-aminoacetophenone [18] and then converted into 3-iodoacetophenone.[19] The iodo-compound (2 g.) was heated with copper bronze (2 g.) (oil-bath at 240—260°) for ½ hr. and the product extracted with boiling ethyl acetate, giving a crude solid which was sublimed at 140—150°/1 mm. and recrystallised from ethyl acetate. 3 : 3′-Diacetyldiphenyl was obtained as colourless needles (350 mg.), m. p. 121—122°. Simpson *et al.*[20] prepared this compound as a by-product in the conversion of 3-aminoacetophenone into 3-chloroacetophenone by the diazonium reaction and described it as pale brown prisms, m. p. 123—124°.

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[17] *Org. Synth.*, Coll. Vol. II, 1943, p. 434.
[18] Morgan and Moss, *J. Soc. Chem. Ind.*, 1923, **42**, 461.
[19] Evans, Morgan, and Watson, *J.*, 1935, 1167.
[20] Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646.

XUM

546. *Diphenylenes. Part III.*[1] *Substitution in the Nucleus.*

By Wilson Baker, J. W. Barton, and J. F. W. McOmie.

A study has been made of substitution in the nucleus of diphenylene. Under carefully defined conditions it has been found possible to effect monosubstitution in the cases of acetylation, nitration, chlorination, bromination, iodination, acetoxymercuration, hydroxylation with lead tetra-acetate, and oxidative coupling, and in all these reactions a 2-substituted diphenylene results. The compounds have been orientated by direct comparison with, or by conversion into, a diphenylene of known orientation, or by reductive cleavage to give one or two diphenyls whose structures are known or now established. Dinitration and diacetylation are shown to occur in positions 2 and 6, corresponding to *meta*-substitution with respect to the first group introduced; this indicates a considerable degree of conjugation between the two benzene rings *via* the four-membered ring.

These findings are discussed in the light of theoretical predictions.

Some reactions involving substitution in diphenylene were described in Part I[2] of this series, and it was shown that acetylation under Friedel–Crafts conditions gave 2-acetyldiphenylene and a diacetyl derivative thought to be the 2 : 6-diacetyl compound. It was also shown that acetoxylation by lead tetra-acetate gave, after hydrolysis, a 1·5% yield of a hydroxydiphenylene, and that sulphonation at room temperature gave a disulphonic acid. The hydroxy-compound has since been shown[1] to be 2-hydroxydiphenylene, but the disulphonic acid has only been orientated by analogy; it is probably, the 2 : 6-disulphonic acid. The present paper describes further substitutions in diphenylene.

Acetylation.—The orientation of the acetyldiphenylene described in Part I[2] as 2-acetyldiphenylene was established by reductive cleavage of the four-membered ring with Raney nickel. This occurs in both of the possible ways, to give a mixture of 3- and 4-acetyldiphenyl, identified chromatographically as their 2 : 4-dinitrophenylhydrazones. 1-Acetyldiphenylene under these conditions would be expected to give a mixture of 2- and 3-acetyldiphenyl, but could give no 4-acetyldiphenyl.

Additional evidence concerning the structure of the acetyldiphenylene (VII) has now been obtained by converting it into the related amine (III), either directly by a Schmidt reaction with sodium azide, or by Beckmann transformation of its oxime (I) and hydrolysis of the resulting acetamido-compound[2] (II). This amine is identical with that prepared by reduction of 2-nitrodiphenylene (IV) synthesised by an unambiguous method.[1] 2-Aminodiphenylene does not undergo diazotisation in the normal manner in aqueous solution; insoluble, probably coupled products are formed.

The diacetyldiphenylene[2] which is also obtained by direct acetylation and was provisionally regarded as 2 : 6-diacetyldiphenylene (VI) was reduced by Raney nickel in alcohol to a single product in 70% yield, namely, 3 : 4′-diacetyldiphenyl, identical with a specimen synthesised by an unambiguous route.[1] The reductive cleavage of 2 : 6-diacetyldiphenylene (VI) could give only 3 : 4′-diacetyldiphenyl irrespective of which of the two central bonds was broken, and the high yield of this single product is a strong argument in support of the 2 : 6-orientation. The only other isomer which could yield 3 : 4′-diacetyldiphenyl is 1 : 7-diacetyldiphenylene and this would be expected to give, in addition, 2 : 3′-diacetyldiphenyl which is not in fact found.

The 2 : 6-orientation has been confirmed by a study of the infrared spectra of the diacetyldiphenylene, of diphenylene itself,[3] and of the following diphenylene derivatives of known orientation: 2-acetyl and its oxime, 2-acetamido, 2-amino, 2-bromo, 2-methoxy, 2-cyano, 2-carboxylic acid, 2 : 6-dinitro, and 1 : 8-dimethoxy. The spectrum of the

[1] Part II, Baker, Barton, and McOmie, preceding paper.
[2] Part I, Baker, Boarland, and McOmie, *J.*, 1954, 1476.
[3] Wittig and Lehmann, *Chem. Ber.*, 1957, **90**, 880.

diacetyl derivative shows a strong band at 832 cm.$^{-1}$, characteristic of a 1 : 2 : 4-trisubstituted benzene. If the compound were 1 : 7-diacetyldiphenylene, strong bands at 830 ± 30 and 780 ± 30 cm.$^{-1}$ would be expected, corresponding to 1 : 2 : 4- and 1 : 2 : 3-trisubstituted benzene rings respectively, but the second band is absent. In all the compounds mentioned the benzene rings appear to contribute independently to the spectrum: a similar effect has been established for the substituted naphthalenes,[4] so that the method may be used to determine the position of substituents.

Nitration.—Diphenylene is readily attacked by nitric acid in acetic acid, but the isolation of individual substances is not easy, and alkali-soluble oxidation products are formed. Nitration with 1·5 equivalents of nitric acid in acetic anhydride at 0° gave a 23·5% yield of 2-nitrodiphenylene (IV), identical with the unambiguously synthesised material.[1] Reduction of the 2-nitrodiphenylene gave 2-aminodiphenylene (III), identical with that prepared from 2-acetyldiphenylene (VII).

Nitration with nitric–sulphuric acid mixture required the use of 72% sulphuric acid to minimise sulphonation of the diphenylene, and the reaction was again complex, giving 2-nitrodiphenylene, 2 : 6-dinitrodiphenylene (V), and a trace of a high-melting hydrocarbon which proved to be 2 : 2′-bisdiphenylenyl (XVIII) formed by an oxidative coupling. The 2 : 6-dinitrodiphenylene was identified by direct comparison with a specimen previously synthesised by an unambiguous method.[1] The hydrocarbon, which was also obtained (2·5% yield) when diphenylene was treated with nitric acid in a sulphuric–acetic acid mixture, was identical with 2 : 2′-bisdiphenylenyl prepared from 2-iododiphenylene (see below) under the conditions of the Busch coupling reaction (hydrazine hydrate, methanolic potassium hydroxide, and a palladium–calcium carbonate catalyst).[5]

Acetoxymercuration.—Diphenylene is converted into 2-acetoxymercuridiphenylene (XIII) in 79% yield (allowing for recovered diphenylene) by heating it with mercuric acetate in acetic acid.[6] The position of the acetoxymercuri-group is proved by ready conversion, by bromine in boiling chloroform, into a bromodiphenylene identical with synthetic 2-bromodiphenylene[1] (XII).

This 2-acetoxymercuridiphenylene is a readily accessible and useful intermediate for the preparation of a variety of 2-substituted diphenylenes. When treated in chloroform with hydrochloric acid and sodium chlorate it gave 2-chlorodiphenylene (XIV) in 82% yield, and when heated with iodine–potassium iodide solution it gave 2-iododiphenylene (XVII). The 2-iododiphenylene, thus readily accessible, was converted into 2-cyanodiphenylene (XVI) when heated with cuprous cyanide in pyridine, and thence by hydrolysis into diphenylene-2-carboxylic acid (XI) identical with the acid previously obtained by oxidising 2-acetyldiphenylene (VII) with sodium hypochlorite.[2] The iodo-compound was also converted into diphenylene-2-carboxylic acid though in poor yield, by passing carbon dioxide into the derived Grignard reagent; a little 2 : 2′-bisdiphenylenyl (XVIII) was also formed at the same time.

Chlorination.—Direct chlorination of diphenylene in carbon tetrachloride in presence of iodine gave complex mixtures, but rather unexpectedly 2-chlorodiphenylene (XIV) was readily obtained in good yield when diphenylene was boiled with iodine monochloride in acetic acid. Only chlorodiphenylene and no iododiphenylene was produced, even when iodine monochloride and half its weight of free iodine were used. The 2-chlorodiphenylene was identical with that prepared *via* 2-acetoxymercuridiphenylene (XIII).

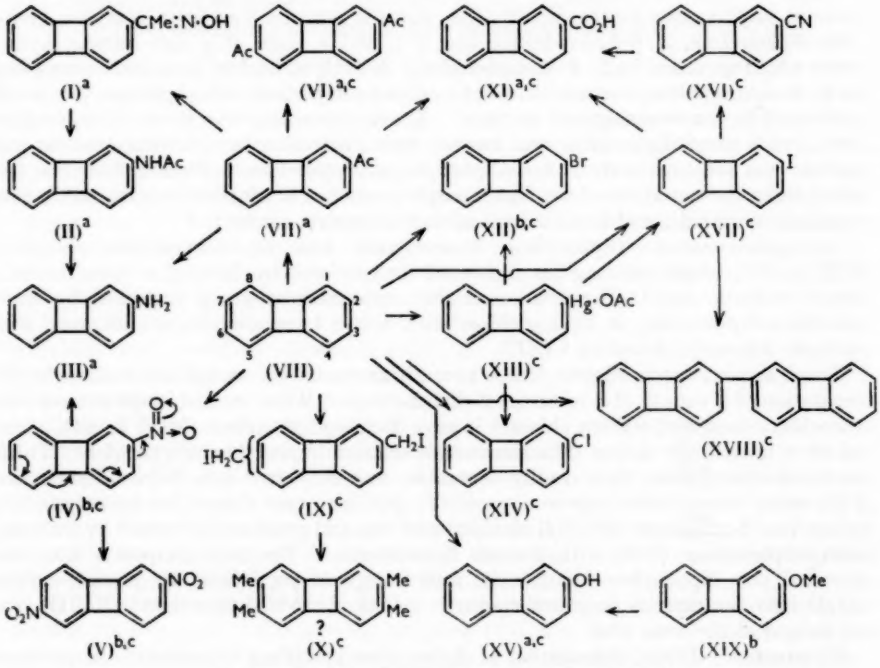
Bromination.—Diphenylene reacts with bromine in carbon tetrachloride in presence of pyridine as a catalyst, to give a 49% yield of 2-bromodiphenylene (XII), identical with that previously synthesised by an unambiguous method[1] or prepared from the acetoxymercuri-compound (XIII) as described above. The bromo-compound is conveniently isolated by means of its complex with 2 : 4 : 7-trinitrofluorenone. Use of

[4] Hawkins, Ward, and Whiffen, *Spectrochim. Acta*, 1957, **10**, 105.
[5] Busch and Weber, *J. prakt. Chem.*, 1936, **146**, 1.
[6] Kobe *et al.*, *Ind. Eng. Chem.*, 1941, **33**, 170; 1942, **34**, 309; 1946, **38**, 247, 248.

excess of bromine led to 2-bromodiphenylene and a substance, m. p. 136—137°, probably a tetrabromo-derivative, which is being investigated further.

Iodination.—Direct iodination of diphenylene with iodine in acetic acid in presence of iodic acid gave a 5% yield of 2-iododiphenylene (XVII), but a 20% yield was obtained when sodium persulphate was used in place of the iodic acid. The product was identical with that prepared by the more convenient reaction *via* 2-acetoxymercuridiphenylene (XIII).

Iodomethylation.—Attempted chloromethylation [7] of diphenylene gave complex mixtures, but iodomethylation took place readily when diphenylene in acetic acid was treated with chlorodimethyl ether and concentrated hydriodic acid. The product was an unstable bisiodomethyl derivative, probably 2 : 6- or 2 : 7-bisiodomethyldiphenylene (IX), characterised as the dipicrate of the related bisthiuronium derivative prepared by reaction of the di-iodo-compound with thiourea.



[a] Part I, ref. 2. [b] Part II, ref. 1. [c] This paper.

An unexpected result was obtained when an attempt was made to reduce the bisiodomethyl derivative to a dimethyldiphenylene with zinc and hydrogen chloride in acetic acid. Analysis of the high-melting product and of its complex with 2 : 4 : 7-trinitrofluorenone showed that it was probably a tetramethyldiphenylene, perhaps the 2 : 3 : 6 : 7-derivative (X), which must have been formed as the result of a type of dismutation involving migration of iodomethyl groups.

The ultraviolet absorption spectra characteristics of most of the diphenylenes and of certain diphenyls described in this paper and in Part II [1] are recorded in the Table.

The spectra of diphenylene and some of its derivatives were illustrated in Part I, and

[7] Review by Fuson and Keever, *Org. Reactions*, 1942, **1**, 63.

it was pointed out that the spectra of the other diphenylenes there described resembled in general that of the parent compound except for loss of fine structure and bathochromic shifts. This resemblance is also shown by the diphenylenes described in Part II and in

Ultraviolet absorption maxima in ethanol.

Diphenylene derivs.	λ (mμ)	$\log_{10}\varepsilon$	λ (mμ)	$\log_{10}\varepsilon$	λ (mμ)	$\log_{10}\varepsilon$
1-Methyl	242	4·66	326	3·31	339	3·58
	251	4·91	331	3·29	343	3·57
					358	3·75
2-Methyl	242	4·74	298	3·13	361	3·88
	250	4·93	343	3·80		
2-Methoxy	253	4·61	306	3·27	338	3·18
	275	4·22	324	3·08	356	3·17
1-Methoxy	253	4·01	345	3·02	360	3·07
					363	3·07
1 : 8-Dimethoxy	256	4·73	303	3·02	335	3·05
	265	4·97	318	3·09	350	2·82
2 : 7-Dimethoxy	245	5·03	342	4·16	360	4·25
	254	5·21				
2-Hydroxy	253	4·64	347	3·72	364	3·82
2-Nitro	232	4·19	264	4·14	348	3·32
	239	4·18	328	3·17	364	3·51
					400	3·44
2 : 6-Dinitro	258	3·88	304	3·67	365	3·34
					382	3·45
2-Bromo	245	4·59	253	4·79	344	3·61
					363	3·76
2 : 6-Diacetyl	219	3·87	286	4·34	376	3·79
	261	4·24	359	3·62		
2-Chloro	244	4·49	252	4·72	344	3·54
					363	3·66
2-Iodo	257	4·82	345	3·79	364	3·95
2-Cyano	252	5·00	334	3·56	362	4·01
	259	5·11	347	3·84	352	3·93
Tetramethyl	246	4·80	256	5·02	372	4·09
2 : 2′-Bisdiphenylenyl	247	4·25	289	4·34	372	3·90
	280	4·45	358	3·79		
Diphenyl derivs.						
3 : 4′-Diacetyl	253	4·41	277	4·50	—	—
3 : 3′-Diacetyl	236	4·81	295	3·61	—	—
4 : 4′-Diacetyl [8]	294	4·63	—	—	—	—

this paper (see Table) except for 1-methoxy-, 1 : 8-dimethoxy-, 2-nitro-, and 2 : 6-dinitro-diphenylene, the spectra of which in 95% ethanol are shown in Figs. 1 and 2. [*Note.* In Part I, Fig. 2, the scale on the right-hand side (for 2-acetyldiphenylene) was accidentally omitted; it should have duplicated that on the right of Fig. 1.]

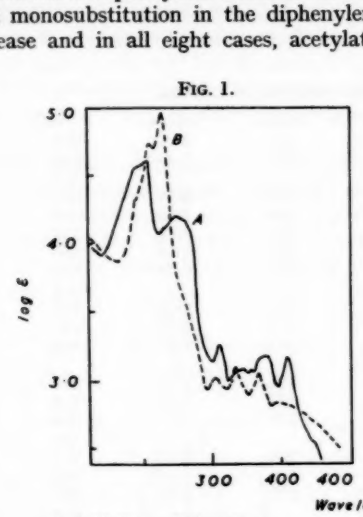
Discussion

Because of its unusual, yet simple structure diphenylene has been the subject of many theoretical calculations, including resonance energy, strain energy, bond lengths, bond orders, and free valencies; references are given by Baker and McOmie.[9] Brown has predicted that diphenylene should undergo electrophilic and nucleophilic substitution more readily than benzene,[10] and these and other considerations by Alonzo and Domingo [11] and Alonzo and Peradejordi [12] have shown that electrophilic, nucleophilic, and homolytic reactions should all occur preferentially at position 2, in spite of the fact that the value of the free valence is greatest in position 1.

[8] Long and Henze, *J. Amer. Chem. Soc.*, 1941, **63**, 1939.
[9] Baker and McOmie, in "Non-benzenoid Aromatic Compounds," Ed. D. Ginsburg, Interscience Publ. Inc., New York, 1958.
[10] Brown, *Trans. Faraday Soc.*, 1950, **46**, 146.
[11] Alonzo and Domingo, *Anales real. Soc. espan. fis. quim.*, 1955, **51**, *B*, 447.
[12] Alonzo and Peradejordi, *ibid.*, 1954, **50**, *B*, 253.

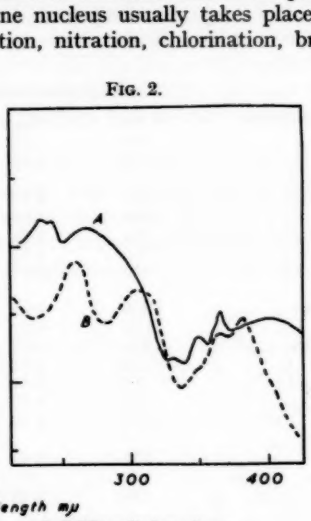
The reactions of diphenylene described in Part I of this series and in the present paper show that monosubstitution in the diphenylene nucleus usually takes place with considerable ease and in all eight cases, acetylation, nitration, chlorination, bromination,

FIG. 1.



A, 1-Methoxydiphenylene.
B, 1 : 8-Dimethoxydiphenylene.

FIG. 2.



A, 2-Nitrodiphenylene.
B, 2 : 6-Dinitrodiphenylene.

iodination, mercuration, hydroxylation with lead tetra-acetate, and oxidative coupling, substitution occurs in position 2. This does not imply that monosubstitution products are either produced in high yield or are easy to isolate. Indeed the high reactivity of the nucleus frequently leads to disubstituted derivatives, *e.g.*, a disulphonic acid (unorientated) with cold concentrated sulphuric acid,[2] or to the formation of by-products.

It is necessary to consider the mechanism of these reactions when comparing the results with the theoretical predictions. The Friedel–Crafts acetylation is an electrophilic substitution,[13] though the reaction is not quite simple because its course may be influenced by changes in temperature and solvent. However, nitration, bromination catalysed by pyridine, and iodination are electrophilic reactions, so that Brown's prediction [10] and those of Alonzo and Domingo [11] are confirmed. It is probable that chlorination with iodine monochloride, and acetoxymercuration, are also electrophilic in character, although mercuric acetate in acetic acid may react by a homolytic mechanism.[14] The acetoxylation of polycyclic hydrocarbons by lead tetra-acetate is considered to be a homolytic reaction,[15] and the poor yield of 2-hydroxydiphenylene obtained by this method confirms Brown's prediction that diphenylene should be almost as unreactive as benzene towards free radicals,[16] but that substitution should occur in position 2.[10] It may be noted that diphenylene does not react with the homolytic reagent *N*-bromosuccinimide even in the presence of benzoyl peroxide.

The only two disubstitution products whose structures are known have the 2 : 6-orientation, the entry of the second group corresponding to a *meta*-position with regard to the first, as shown in formula (IV). Diacetylation and dinitration of diphenylene give 2 : 6-diacetyldiphenylene (VI) and 2 : 6-dinitrodiphenylene (V) respectively. The dinitration proceeds in only 4% yield and traces of other isomers may have been formed,

[13] Badger, "The Structure and Reactions of the Aromatic Compounds," Cambridge Univ. Press, 1954.
[14] Ingold, "Structure and Mechanism in Organic Chemistry," Bell and Sons, Ltd., London, 1953, p. 304.
[15] Waters, "Chemistry of Free Radicals," 2nd edn., Oxford, 1948.
[16] Brown, *Trans. Faraday Soc.*, 1949, **45**, 300.

but the diacetylation proceeds in high yield and despite a careful search for other isomers none was found. Hence, the presence of a *meta*-directing substituent in one six-membered ring controls the position taken up by a second substituent which, as would be expected, enters the other benzene ring but not at random. This shows that there is a considerable degree of resonance interaction between the two benzene rings, and there must be in consequence some *cyclo*butadienoid character in the four-membered ring. This conclusion is noteworthy in view of the fact that acetylation of 4-acetyldiphenyl gives 4 : 4′-diacetyldiphenyl instead of 4 : 3′-diacetyldiphenyl which should be formed if there were effective conjugation between the two aromatic nuclei.[17] The greater conjugation between the two benzene rings in diphenylene than in diphenyl may be ascribed to the facts that diphenylene is a rigid planar molecule, whilst diphenyl is to some extent non-planar.

Experimental

2-*Acetyldiphenylene* (VII).—Powdered aluminium chloride (4 g.) was added in portions to a stirred solution of diphenylene (1·0 g.) and acetyl chloride (0·6 g.) in carbon disulphide (250 ml.). After being stirred for 3 hr. the mixture was kept for 8 hr., then shaken with cold, dilute hydrochloric acid, and the product, collected in carbon disulphide, was sublimed at 120—130°/12 mm., giving 2-acetyldiphenylene (0·845 g.), m. p. 132—134°. A trace of 2 : 6-diacetyldiphenylene remained undissolved in the carbon disulphide.

2-*Aminodiphenylene* (III) (for method cf. Dice and Smith [18]).—Finely powdered sodium azide (0·10 g.) was added to a mixture of 2-acetyldiphenylene (0·10 g.), trichloroacetic acid (2 g.), and tetraphosphoric acid (1 g.) at 70—80°, and after ½ hr. a further portion of sodium azide (0·10 g.) was added, and the heating continued for 6 hr. Dilution with water gave a solid which was boiled for 1 hr. with hydrochloric acid (10 ml.), water (10 ml.), and ethanol (2 ml.), then basified with sodium hydroxide, and extracted with ether. The ether yielded a solid which was sublimed at 115—120°/10 mm., giving 2-aminodiphenylene (0·037 g.; m. p. 119—120°; the pure compound has m. p. 123—124° [2]).

2 : 6-*Diacetyldiphenylene* (VI).—Powdered aluminium chloride (1·0 g.) was added in portions to a well-stirred solution of diphenylene (0·30 g.) in carbon disulphide (40 ml.) and acetyl chloride (1·0 g.). The mixture was stirred for a further 3 hr. and kept for 8 hr., then cold hydrochloric acid was added, and the solid 2 : 6-diacetyldiphenylene was collected; after one crystallisation from ethanol it formed deep yellow needles (0·30 g.), m. p. 243—245° (the pure compound has m. p. 247—248° [2]).

Reduction of 2 : 6-*Diacetyldiphenylene* (VI) *to* 3 : 4′-*Diacetyldiphenyl*.—2 : 6-Diacetyldiphenylene (0·30 g.) was refluxed for 1 hr. in ethanol (25 ml.) with Raney nickel (*ca.* 0·5 g.). The now colourless solution was filtered, the nickel washed with hot ethanol (25 ml.), the combined solutions evaporated, the residue sublimed at 130—140°/0·1 mm. (yield, 0·21 g.), and crystallised from ethanol, giving colourless needles, m. p. 100—101°. The m. p. was not depressed on admixture with authentic 3 : 4′-diacetyldiphenyl, m. p. 101—102°, described in Part II.[1]

2-*Nitrodiphenylene* (IV) *and* 2-*Aminodiphenylene* (III).—Nitric acid (0·2 ml.; *d* 1·42; 1·6 equivs.) in acetic acid (2 ml.) was added to a stirred solution of diphenylene (0·30 g.) in acetic anhydride (10 ml.) at 0°. After ½ hr. the cooling-bath was removed, and the mixture allowed to reach room temperature (¾ hr.), poured into water, neutralised with sodium hydrogen carbonate, and steam-distilled. The distillate (1 l.) contained 2-nitrodiphenylene as deep yellow needles (0·09 g.), m. p. 105—106·5° either alone or mixed with the specimen previously prepared.[1]

2-Nitrodiphenylene (21 mg.) was boiled for ½ hr. with ethanol (0·5 ml.), concentrated hydrochloric acid (1 ml.), and stannous chloride (250 mg.), and the mixture then made alkaline with sodium hydroxide and steam-distilled. The solid was extracted into light petroleum (b. p. 40—60°), giving 2-aminodiphenylene (13 mg.; m. p. 120—121°), which after recrystallisation from the same solvent formed yellow needles, m. p. 123—124°, alone or mixed with a specimen prepared as previously described.[2,1]

2 : 6-*Dinitrodiphenylene* (V) *and* 2 : 2′-*Bisdiphenylenyl* (XVIII).—Powdered diphenylene

[17] Ferriss and Turner, *J.*, 1920, **117**, 1147.
[18] Dice and Smith, *J. Org. Chem.*, 1949, **14**, 179.

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(300 mg.) was added in portions to a stirred mixture of nitric acid (0·15 ml.; *d* 1·42; 1·2 equivs.), concentrated sulphuric acid (0·75 ml.), and water (0·25 ml.) at 0°; the mixture was then removed from the cooling-bath, and after it had reached room temperature it was diluted, neutralised, and steam-distilled. The distillate yielded a mixture of diphenylene (100 mg.) and 2-nitrodiphenylene (*ca.* 35 mg., 13·5%), the latter being removed and identified by reduction to 2-aminodiphenylene. The product not volatile in steam was sublimed at 220°/12 mm., crystallised from ethanol, giving deep yellow needles and pale yellow plates, then resublimed slowly at 170°/12 mm., and the homogeneous sublimate recrystallised from ethanol. 2 : 6-Dinitrodiphenylene was thus obtained as deep-yellow needles (12 mg., 4%) which sublimed above 260° (Found: C, 59·7; H, 2·9; N, 11·6. $C_{12}H_6O_4N_2$ requires C, 59·5; H, 2·5; N, 11·6%). The ultraviolet spectrum was identical with that of the orientated material.

The few mg. of material which did not sublime at 170°/12 mm. separated from ethanol in pale yellow leaflets, m. p. 240—242°, and proved to be 2 : 2′-bisdiphenylenyl (XVIII). This product was also obtained when diphenylene (300 mg.), suspended in a mixture of concentrated sulphuric acid (5 ml.) and acetic acid (5 ml.), was treated with nitric acid (0·2 ml.; *d* 1·42; 1·6 equivs.) in sulphuric acid (5 ml.) at 0° for ¾ hr. with stirring, and then at room temperature for 1 hr. It was isolated and crystallised as before (5 mg.) and had m. p. 242—243°. The m. p. was not depressed on admixture with a specimen prepared from 2-iododiphenylene (below).

2-*Acetoxymercuridiphenylene* (XIII).—The yellow solution obtained by heating diphenylene (300 mg.) and mercuric acetate (650 mg.) in acetic acid (10 ml.) on the water-bath for 2 hr. was diluted, and unchanged diphenylene (212 mg.) removed by rapid steam-distillation. The non-volatile material was collected at 0° and extracted with warm benzene in a Soxhlet apparatus, giving 2-*acetoxymercuridiphenylene* (187 mg.) which crystallised from benzene as a yellow powder, m. p. 176—177° (Found: C, 40·8; H, 2·7. $C_{14}H_{10}O_2Hg$ requires C, 40·9; H, 2·4%).

2-*Chlorodiphenylene* (XIV).—2-Acetoxymercuridiphenylene (180 mg.) was stirred with concentrated hydrochloric acid (50 ml.) and chloroform (25 ml.), and a saturated aqueous solution of potassium chlorate (20 mg.) was added dropwise. After ½ hr. a further portion of potassium chlorate (5 mg.) was similarly added, and stirring was continued for 4 hr. The chloroform layer was washed with aqueous sodium carbonate, and the product sublimed (crude material, 56 mg.; m. p. 56—60°), converted into the 2 : 4 : 7-trinitrofluorenone complex (scarlet needles, m. p. 133—134°), regenerated, and resublimed as in the preparation of 2-iododiphenylene. Pure 2-*chlorodiphenylene* forms very pale yellow plates, m. p. 67·5—68·5° (Found: C, 77·6; H, 3·9; Cl, 17·9. $C_{12}H_7Cl$ requires C, 77·3; H, 3·8; Cl, 19·0%).

2-*Bromodiphenylene* (XII).—2-Acetoxymercuridiphenylene (400 mg.), suspended in chloroform, was treated with bromine in chloroform (3 ml. of a solution of 1 ml. of bromine in 50 ml. of chloroform). After ½ hr. the almost colourless solution was washed with aqueous sodium hydrogen sulphite, and the chloroform layer yielded a residue which was sublimed at 110—120°/13 mm., giving a crude product (178 mg.; m. p. 54—58°) which was purified as the 2 : 4 : 7-trinitrofluorenone complex (scarlet needles, m. p. 136—137°) and regenerated and resublimed as in the preparation of 2-iododiphenylene. The pure 2-*bromodiphenylene* formed pale yellow plates, m. p. 64—65° (Found: C, 62·1; H, 3·2; Br, 35·0. $C_{12}H_7Br$ requires C, 62·4; H, 3·0; Br, 34·6%). The m. p. was not depressed on admixture with authentic 2-bromodiphenylene synthesised as described in Part II.[1]

2-*Iododiphenylene* (XVII).—2-Acetoxymercuridiphenylene (400 mg.), suspended in a solution of iodine (1 g.) in 10% aqueous potassium iodide, was stirred for ½ hr. at 60—70°, treated with an excess of sodium hydrogen sulphite, and steam-distilled. The pale yellow solid in the distillate was extracted into light petroleum (b. p. 40—60°), giving a crude product (216 mg.; m. p. 53—56°) which was treated with the calculated quantity of 2 : 4 : 7-trinitrofluorenone in ethanol–acetic acid, and the solid was then recrystallised from ethanol, giving the deep scarlet complex, m. p. 132·5—134°. Decomposition of this complex (100 mg.) by passing its benzene solution through alumina (20 × 2 cm.), elution with the same solvent, and sublimation at 110—120°/12 mm. gave 2-*iododiphenylene* (44 mg.) as pale yellow plates, m. p. 64·5—65·5° (Found: C, 51·8; H, 2·1; I, 45·6. $C_{12}H_7I$ requires C, 51·8; H, 2·5; I, 45·7%).

2-*Cyanodiphenylene* (XVI).—2-Iododiphenylene (200 mg.) was heated under reflux for 10 hr. in an oil-bath at 140—150° with anhydrous cuprous cyanide (150 mg.) and pyridine (1 ml.), and the product extracted alternately with hot benzene and aqueous ammonia (*d* 0·880

diluted with an equal volume of water). The united benzene extracts yielded a product which was sublimed at 120—130°/11 mm. (115 mg.; m. p. 60—85°), crystallised from light petroleum (b. p. 40—60°), and resublimed, giving *2-cyanodiphenylene* as yellow plates (98 mg.), m. p. 99—100° (Found: C, 87·8; H, 4·0; N, 7·8. $C_{13}H_7N$ requires C, 88·1; H, 4·0; N, 7·9%).

Diphenylene-2-carboxylic Acid (XI).—(*a*) 2-Cyanodiphenylene (60 mg.) was boiled for 2 hr. with 20% aqueous sodium hydroxide (10 ml.) and ethanol (10 ml.); hot water (80 ml.) was then added, and the solution was filtered and acidified. The yellow solid was collected, sublimed at 150—160°/12 mm. (57 mg.; m. p. 216—218°) and crystallised from aqueous methanol, giving diphenylene-2-carboxylic acid as yellow prisms, m. p. 221—222°, alone or on admixture with a sample prepared from 2-acetyldiphenylene by treatment with sodium hypochlorite.[2]

(*b*) No reaction occurred between 2-iododiphenylene (150 mg.) and magnesium (250 mg.) in ether (2 ml.) till methyl iodide (0·5 ml.) was added in portions. After being boiled for ½ hr. the solution was poured on solid carbon dioxide, and the acidic material (5 mg.) was later isolated in the usual way. Sublimation and recrystallisation from light petroleum (b. p. 40—60°) gave the slightly impure acid, m. p. 215—218°. From the neutral product of the reaction was isolated by sublimation at 130°/12 mm. 2-iododiphenylene (106 mg.), and at 190—210°/12 mm. 2 : 2′-bisdiphenylenyl (XVIII), m. p. and mixed m. p. 240—242°.

2 : 2′-Bisdiphenylenyl (XVIII).—A mixture of 2-iododiphenylene (150 mg.), 1% palladium–calcium carbonate[5] (500 mg.), hydrazine hydrate (100 mg.), 5% methanolic potassium hydroxide (10 ml.), and water (1 ml.) was boiled for 1 hr. After filtration through a Soxhlet thimble the solution was brought to neutrality with concentrated hydrochloric acid, ethanol was added, the mixture was refiltered through the Soxhlet thimble, and the contents of the thimble were then extracted for 6 hr. with hot ethanol. Concentration of the extract gave a solid which was sublimed, giving at 100—120°/12 mm. diphenylene (crude 48 mg.), and at 180—200°/0·5 mm. a yellow solid (18 mg.; m. p. 210—230°) which after crystallisation from ethanol gave yellow leaflets of *2 : 2′-bisdiphenylenyl* (12 mg.), m. p. 242·5—243·5° (Found: C, 95·5; H, 4·7. $C_{24}H_{14}$ requires C, 95·4; H, 4·6%).

Chlorination of Diphenylene.—Diphenylene (500 mg.), iodine monochloride (1 g.), and acetic acid (30 ml.) were heated (oil-bath at 120—130°) for 6 hr., and steam-distilled after addition of water and excess of sodium hydrogen sulphite. The distillate was rendered alkaline, and the solid (470 mg.; m. p. 51—56°) collected with ether and sublimed, giving a trace of diphenylene at 80°/12 mm. and 2-chlorodiphenylene at 110—120°/12 mm. Two crystallisations from aqueous methanol gave the pure compound as very pale yellow plates (355 mg.), m. p. and mixed m. p. with a specimen prepared from 2-acetoxymercuridiphenylene, 66—67°.

Bromination of Diphenylene.—A solution of bromine in carbon tetrachloride (9 ml.; made from 1 ml. of bromine and 50 ml. of carbon tetrachloride) was added to diphenylene (500 mg.), and the slow reaction was hastened by the addition of a drop of pyridine. After 10 min. a further amount of the bromine solution (5 ml.) was added, and the mixture warmed on the water-bath for 15 min. The solution was shaken with aqueous sodium hydrogen carbonate and more carbon tetrachloride, dried and distilled, giving a trace of diphenylene and then an oil, b. p. 120—130°/2 mm., which partly solidified. This crude 2-bromodiphenylene (530 mg.) was converted into the 2 : 4 : 7-trinitrofluorenone complex (890 mg.; m. p. 135—137°); the pure compound was regenerated therefrom as previously described and finally sublimed as pale yellow plates, m. p. and mixed m. p. with a specimen prepared from 2-acetoxymercuridiphenylene, 64—65°.

Iodination of Diphenylene.—(a) *Using iodine and sodium persulphate.* Diphenylene (200 mg.), iodine (300 mg.), sodium persulphate (1 g.), and acetic acid (10 ml.) were boiled for 16 hr., diluted, and steam-distilled. The distillate was extracted with ether, and the extracts, after being washed with aqueous sodium carbonate, yielded a product which was sublimed at 80°/14 mm. to remove diphenylene (127 mg.), then at 130—140°/14 mm., giving crude 2-iododiphenylene (32 mg.; m. p. 55—60°) which was purified *via* the 2 : 4 : 7-trinitrofluorenone complex and by final sublimation. The pure compound had m. p. and mixed m. p. with a specimen prepared from 2-acetoxymercuridiphenylene, 63—64°.

(b) *Using iodine and iodic acid.* A similar experiment using iodic acid instead of sodium persulphate and a reaction time of 2 hr. similarly gave unchanged diphenylene (107 mg.) and crude 2-iododiphenylene (12 mg.).

Iodomethylation of Diphenylene.—To diphenylene (100 mg.) in acetic acid (12 ml.) were added 90% chloromethyl methyl ether (4 ml.) and hydriodic acid (10 ml.; *d* 1·7); after 24 hr.

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the bright yellow solid was collected, washed with acetic acid, and dried (155 mg.). This substance, probably 2 : 7- or 2 : 6-bisiodomethyldiphenylene (IX), decomposes above 86° with liberation of iodine and could not be satisfactorily crystallised. It was therefore heated with thiourea (200 mg.) in ethanol (4 ml.) for ½ hr. and the hot solution treated with picric acid (200 mg.), giving the related *bisthiuronium dipicrate*, $C_{12}H_6(C_2H_5N_2S,C_6H_3O_7N_3)_2$ as an orange powder which was purified by digestion with boiling ethanol; it had m. p. 204—206° (decomp.) (Found: C, 43·2; H, 3·1; N, 17·7. $C_{28}H_{22}O_{14}N_{10}S_2$ requires C, 42·8; H, 2·8; N, 17·8%).

2 : 3 : 6 : 7-*Tetramethyldiphenylene* (X).—The crude bisiodomethyldiphenylene described above (390 mg.) was added to acetic acid (100 ml.) and zinc dust (0·5 g.), and the mixture was stirred and hydrogen chloride passed through at 50° for 4½ hr. with addition of more zinc dust after 1½ hr. and 3 hr. The filtered solution was diluted, and the solid collected and sublimed at 130—140°/10 mm. (57 mg.; m. p. 200—210°). The *complex* with 2 : 4 : 7-trinitrofluorenone prepared in, and crystallised from, ethanol forms deep brown needles, m. p. 171—172° (Found: C, 66·3; H, 3·7; N, 8·4. $C_{29}H_{21}O_7N_3$ requires C, 66·5; H, 4·0; N, 8·0%). The complex was decomposed by passing its solution in benzene through an alumina column and eluting this with benzene; sublimation followed by crystallisation from ethanol gave the 2 : 3 : 6 : 7-*tetramethyldiphenylene* as straw-coloured needles, m. p. 222·5—223·5° (Found: C, 92·1, 92·2; H, 7·6, 8·0. $C_{16}H_{14}$ requires C, 92·3; H, 7·7%).

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The University, Bristol. [*Received, March 21st*, 1958.]

547. *Polarography of Some Aromatic Carbonyl Compounds in Dimethylformamide.*

By P. H. Given, M. E. Peover, and J. Schoen.

Half-wave potentials for the polarographic reduction of anthraquinone and some of its hydroxy-derivatives, 12 : 12′-dimethoxydibenzanthrone, benzaldehyde, acetophenone, benzophenone, xanthone, benzanthrone, and purpurogallin in dimethylformamide are uniformly more negative than those in aqueous solutions, and in most cases two waves are observed. The behaviour when tetraethylammonium iodide is used as supporting electrolyte is consistent with a mechanism involving two one-electron steps. Quinones are reduced to the quinol ions.

As we wanted to study the polarography of oxygen-containing groups in solvent extracts of coals, which are not soluble in the aqueous or partially aqueous media previously used for carbonyl compounds, but are soluble in dimethylformamide, we investigated several aromatic carbonyl compounds, chosen to include a number in which the carbonyl group is strongly conjugated to the aromatic system, in this solvent. Since dimethylformamide does not ionize to yield protons, one would expect a different mechanism from that accepted for aqueous solutions, and different half-wave potentials.

Dimethylformamide was used for the polarography of aromatic hydrocarbons by Wawzonek *et al.*[1] In the present work lithium chloride and tetraethylammonium iodide were used as supporting electrolytes. Some characteristics of these solutions as polarographic media are described; for further details see ref. 2.

Experimental

Materials.—Lithium chloride and dimethylformamide from George and Becker were used as received. The water content of the solvent was 0·02—0·1% (Karl Fischer). Tetraethylammonium iodide was prepared by heating an equimolecular mixture of triethylamine and

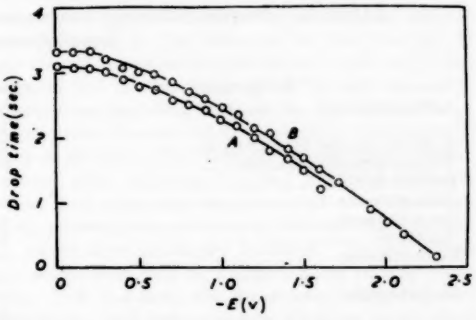
[1] Wawzonek, Blaha, Berkey, and Runner, *J. Electrochem. Soc.*, 1955, **102**, 235.
[2] Given and Peover, *J.*, in the press.

ethyl iodide in nitrobenzene * for 2 hr. at 80°; the salt was precipitated on cooling, and was washed on the filter with much carbon tetrachloride, and repeatedly crystallised from alcohol.

Apparatus.—A Tinsley polarograph, model 14/3, was used with a simple type of cell in which the mercury pool served as anode. The cell had two side-tubes with sintered-glass plates across their mouths for the introduction of oxygen-free nitrogen.

Procedure.—1·0N-Lithium chloride and 0·1N-tetraethylammonium iodide solutions were used. The concentration of reducible substance in these supporting solutions was about 0·1—1·0 mM. Nitrogen (" oxygen-free " from a cylinder) was bubbled for 20 min. through the solutions to remove oxygen. Usually the mercury pool was added *after* this, and nitrogen was then passed for a few more minutes. This procedure was recommended by Arthur and Lyons; [4] its neglect caused the appearance of a spurious wave near 0 v.

Results.—(1) *Polarography in dimethylformamide solutions.* Half-wave potentials are referred to the potential of the mercury pool; this eliminates the risk of contamination introduced by an aqueous calomel electrode and avoids liquid-junction potentials. The potential of the pool against a saturated aqueous calomel electrode was −0·47 v when covered by N-lithium chloride in



Electrocapillarity curves for A, N-lithium chloride; B, 0·1N-tetraethylammonium iodide in dimethylformamide. —E is the potential of the dropping-mercury electrode against the mercury pool.

dimethylformamide and −0·50 v under 0·1N-tetraethylammonium iodide. These values are close to the potential of the pool covered by solutions of tetra-*n*-butylammonium iodide in certain other organic solvents (collected values are discussed by Hoijtink *et al.*[5]). The potential of the pool, when measured in an H-cell against the saturated calomel electrode, remained constant during a polarogram when the pool was the anode and the half-wave potentials of most of the substances studied were independent of concentration. The pool therefore provides a stable and reproducible reference potential. Galvanometer zero was −0·01 v against the pool anode in 0·1N-tetraethylammonium iodide.

We attempted to use a calomel electrode made up in dimethylformamide saturated with lithium chloride (about 2N). The potential of the pool against a freshly-prepared electrode of this kind was reproducibly −0·45 v, but the electrode appeared to be unstable and it is not clear what the potential-determining reaction is.[2] Half-wave potentials of anthraquinone measured in an H-cell with a dimethylformamide–calomel electrode as anode are included in Table 2. The first and second waves were 0·465 and 0·48 v respectively more negative than the values referred to the mercury pool.

Electrocapillarity curves with lithium chloride and tetraethylammonium iodide as the base electrolytes are shown in the Figure. The curves are similar to that reported by Bergman [6] for tetrabutylammonium iodide–2-methoxyethanol solutions and are not quite the usual inverted parabolas. The maxima occur near 0 v (referred to the pool anode). The drop time in tetraethylammonium iodide becomes extremely short at potentials more negative than

* The use of nitrobenzene as a solvent in the preparative use of the Menschutkin reaction is, we believe, new. It is well known (see for example Laidler [3]) that the reaction velocity in certain solvents, of which nitrobenzene is one, is 100—1000 times higher than it is in the more common aliphatic solvents. We have used the same procedure with success in the preparation of the higher tetra-alkylammonium iodides, though there the solubilities of the salts are less convenient.

[3] Laidler, " Chemical Kinetics," McGraw-Hill, New York, 1950, p. 116.
[4] Arthur and Lyons, *Analyt. Chem.*, 1952, **24**, 1422.
[5] Hoijtink, van Schooten, de Boer, and Aalbersberg, *Rec. Trav. chim.*, 1954, **73**, 355.
[6] Bergman, *Trans. Faraday Soc.*, 1954, **50**, 829.

−1·9 v, so diffusion currents of all substances giving half-wave potentials more negative than −1 v were corrected for the change of drop-time with applied potential.

The cell resistance, measured with a Mullard conductivity bridge operating at 3000 c./sec., was about 550 ohms with 0·1N-tetraethylammonium iodide. The iR drop was therefore 0·5—5 mv and was ignored.

(2) *Reduction of carbonyl compounds.* Except for the dibenzanthrone derivative, all the substances gave well-defined waves. The results are collected in Tables 1 and 2. The term A (the diffusion-current constant) is the value of $i_d/(cm^{\frac{2}{3}}t^{\frac{1}{6}})$ where i_d is the diffusion current (μA), c the concentration (mmole l.$^{-1}$), m the mass (mg.) of mercury flowing per sec., and t the drop-time (sec.). Results were obtained for all substances over a range of concentrations; figures for only one representative concentration are given unless the behaviour was concentration-dependent.

Logarithmic analysis of the first waves in some polarograms in lithium chloride and all those in tetraethylammonium iodide gave good straight lines of slope *ca.* 0·059; if the reactions

TABLE 1. *Aromatic carbonyl compounds in tetramethylammonium iodide–dimethylformamide*

Substance	Concn. (mmole/l.)	$-E_{\frac{1}{2}}$ (v)	A
Anthraquinone	0·385	0·33, 0·90	1·75, 1·65
	1·10	0·33, 0·96	1·70, 1·45
1 : 4-Dihydroxyanthraquinone	1·00	0·07, 0·58	2·15, 1·75
1-Hydroxyanthraquinone	0·74	0·16, 0·73	1·75, 1·15
Benzaldehyde	0·43	1·30, 1·83	2·50, 3·10
Acetophenone	0·27	1·49, 1·89	1·70, 3·90
Benzophenone	0·36	1·22, 1·47	1·47, 1·49
Xanthone	0·40	1·15, 1·55, 2·10	1·85, 1·80, 3·0
Benzanthrone	0·36	0·72, 1·30	1·37, 1·64
	1·50	0·74, 1·38	1·26, 1·22
Purpurogallin	0·10	0·89, 1·41, 1·72	1·50, 1·71, 1·36
	1·00	0·87, 1·50	1·56, 1·72

TABLE 2. *Behaviour of some quinones in lithium chloride–dimethylformamide.*

Substance	Concn. (mmole/l.)	$-E_{\frac{1}{2}}$ (v)	A
Anthraquinone	0·80	0·305, 0·57	1·3, 0·86
	0·91	0·77,* 1·05 *	
1 : 4-Dihydroxyanthraquinone	0·20	0·42, 0·83	1·75 (total height)
	0·60	0·42, 0·55, 0·90	
1-Hydroxyanthraquinone	0·385	0·10, 0·54	0·93, 1·20
1 : 2 : 5 : 8-Tetrahydroxyanthraquinone	0·20	0·37, 0·70	0·73, 0·89
12 : 12′-Dimethoxydibenzanthrone	0·28	0·56	1·10

* Potential vs. S.C.E. in dimethylformamide.

were known to be reversible this would indicate that they were one-electron changes. Irregularities in the waves in lithium chloride are discussed later. The second waves gave fairly good straight lines of slope usually *ca.* 0·07—0·08, but with acetophenone it was 0·12, with benzaldehyde 0·11, and with purpurogallin (0·5—1·0 mM) 0·14. The waves for these substances are possibly composite. In tetraethylammonium iodide the half-wave potential of none of the carbonyl compounds, except benzanthrone, anthraquinone, and purpurogallin, varied with concentration, but the relative heights of the waves changed somewhat. Purpurogallin, a benzotropolone, gave three waves in very dilute solution, but at higher concentrations the third could not be resolved. Xanthone also gave three waves, but the third was much larger than the other two. The diffusion currents of anthraquinone gave a straight-line plot against the square-root of the corrected wave-height.

The polarography of anthraquinone was further studied by controlled-potential electrolysis. Anthraquinone (1·5 g.) in 0·1N-tetraethylammonium iodide in dimethylformamide (500 ml.) was electrolysed at −1·1 v (measured against a small mercury pool in the cathode compartment), a stirred mercury pool being used as cathode (area when quiescent 60 cm.^{2}) and a roll of silver

gauze as anode. The two compartments were separated by a fine-porosity sintered-glass disc. The quantity of electricity consumed corresponded to the addition of about 2·4 electrons per molecule. During electrolysis the solution was intensely red, characteristic of alkali-metal salts of 9 : 10-dihydroxyanthracene. This persisted when the current was switched off, provided the solution was not exposed to air. After electrolysis addition of excess of acetic anhydride immediately discharged the colour. From the solution a 75% yield of 9 : 10-diacetoxyanthracene was isolated, whose melting point and polarographic behaviour [7] were identical with those of a sample prepared by reductive acetylation.

When anthraquinone was polarographed in tetraethylammonium iodide solution containing acetic anhydride (*ca.* 20 mM), only one wave was observed, of half-wave potential equal to that of the first wave previously observed and of height equal to the sum of the heights of the two previous waves. Benzophenone and xanthone behaved similarly, but here the half-wave potentials of the single waves were slightly less negative (about 0·1 V) than the values for the first waves observed in the absence of the anhydride.

Anthraquinone and its 1- and 1 : 4-hydroxy-derivatives were studied in both lithium chloride and tetraethylammonium iodide solutions. The behaviour of the first two was similar in both. The first waves given by each substance were more negative in tetraethylammonium iodide–dimethylformamide by an amount approximately equal to the difference in the potential of the pool in the two base solutions (0·04 V); the second waves were considerably more negative; the wave-heights were greater in the iodide solution and the two waves given by each substance were more nearly equal in height. There were some puzzling features in the behaviour of anthraquinone and 1 : 4-dihydroxyanthraquinone in the lithium chloride solution which suggest that this salt is a less satisfactory supporting electrolyte than tetraethylammonium iodide. The half-wave potentials of anthraquinone varied with concentration and the total diffusion current constant was low for a two-electron wave (the latter was also true of all the substances in lithium chloride). The behaviour of 1 : 4-dihydroxyanthraquinone in lithium chloride was complex, since at some concentrations three waves were distinctly resolved. At the lowest concentrations (0·04 and 0·1 mM) the first two waves were seen as a single, fairly regular wave of slope about 0·06. At higher concentrations (0·2—0·4 mM) the wave was composite, but could not be resolved. At the highest concentrations used (0·6—0·8 mM) all three waves were resolved, but not well enough for reliable logarithmic analysis of the first two waves to be made. The slope of the third wave was 0·035, which would correspond to $n = 1·7$ if the reaction were reversible. The relative heights of the waves varied with both concentration and temperature. With increasing concentration the second wave grew at the expense of the other two, so that at 0·8 mM its height was more than double that of either of the others. From 8° to 50° and at 0·3 mM, the height of the third wave decreased with increasing temperature; the temperature coefficient for the total diffusion current was about +1·5% per degree, which is a normal value (see ref. 8, p. 93), and the half-wave potential of the third wave decreased steadily from −0·86 V at 8° to −0·82 V at 50°. The potential of the third wave also shifted somewhat towards more negative values with concentration. On the other hand, 1 : 4-dihydroxyanthraquinone showed only two waves in tetraethylammonium iodide, the first rising immediately from 0 V and the galvanometer zero. The other hydroxyanthraquinone did not show these complexities within the range of conditions used.

Edsberg [9] has studied the polarography of anthraquinone in dimethylformamide with lithium chloride as supporting electrolyte, and reports waves at more negative potentials than ours (−0·83 V and −1·17 V against aqueous S.C.E.) with $i_d/c = 2·0$. However, various acid anhydrides and lithium hydroxide were also present in his solution.

The waves given by 1 : 2 : 5 : 8-tetrahydroxyanthraquinone and 12 : 12′-dimethoxydibenzanthrone (the latter was selected as an example of a complex highly condensed quinone) in lithium chloride solution were superimposed on a steady rise in current and so were somewhat drawn-out (see Fig. 1 in the following paper) and not susceptible to satisfactory logarithmic analysis. The slope of the first wave given by the anthraquinone derivative was about 0·06, but the log $i/(i_d - i)$ plot (where i is the current at any point on the wave) for the single wave given by the dye was linear only over its centre portion, and the slope of this portion was abnormally high (*ca.* 0·1): the wave is perhaps composite.

[7] Given, *J.*, 1958, 2684.
[8] Kolthoff and Lingane, "Polarography," Interscience, New York, 2nd Edn., 1952.
[9] Edsberg, *Analyt. Chem.*, 1953, **25**, 798.

XUM

Discussion

The diffusion constant of anthracene in dimethylformamide has been measured by Coggan and Given [10] by the porous-diaphragm method. The results, taken with polarographic data for the hydrocarbon in the same solvent,[7] indicate that a diffusion current constant of about 4 corresponds to a two-electron addition to a molecule of this size in this solvent. On this basis it can be seen from Table 1 that for all the substances studied the total wave heights (of first two waves only where more than two were observed) are reasonable for two-electron additions (due allowance being made for differences in molecular size and shape). This view is confirmed for anthraquinone by the recovery of a high yield of 9 : 10-diacetoxyanthracene from controlled-potential electrolysis followed by acetylation. The two waves were of roughly equal height (except those of acetophenone), the relative heights did not vary much with concentration, and the i_d/c ratios were constant over a range of concentrations; hence neither wave is due to adsorption on the mercury surface,* and it may be accepted that reduction of the various carbonyl compounds takes place by two one-electron steps. The observed variation of the anthraquinone limiting currents with the height of the mercury reservoir indicates that both waves are diffusion-controlled.

Hoijtink *et al.*[5] have made an illuminating analysis of possible mechanisms of reduction at the dropping-mercury electrode, which, though originally in reference to hydrocarbons, is quite general. They point out that at a voltage above the start of the first wave the ion R^- formed by reversible addition of one electron must suffer one of two fates: either (*a*) diffuse into the bulk of liquid, where $R^- + H^+ \longrightarrow RH$, or (*b*) react with a proton to form a radical RH· which then adds an electron to become RH^-, followed by $RH^- + H^+ \longrightarrow RH_2$. If the basicity of R^- and the availability of protons is such that (*b*) is faster than (*a*), then the RH· radical formed on the electrode surface immediately adds a second electron, with no further change in potential, because, with hydrocarbons at least, the reduction potential of a radical is always less negative than that of the molecule from which it is derived. Consequently only one wave is observed, of height equivalent to a two-electron addition but of slope corresponding approximately to $n = 1$.† On the other hand, if proton addition is slow compared with diffusion away from the electrode surface, two waves are observed, each of slope corresponding to $n = 1$. The second wave corresponds to the addition of a further electron to R^-. Even in dioxan–water mixtures containing 25% of water, proton addition is slow and most hydrocarbons show behaviour of type (*a*).[5,7] Hoijtink *et al.*[5] found that if a proton donor, such as hydrogen iodide, is added in sufficient amount (*e.g.*, 4 mmoles of HI per l.) the height of the second wave becomes very small or vanishes while that of the first increases without great change in half-wave potential, *i.e.*, behaviour changes to type (*b*). Wawzonek *et al.*[1] found the same effect when water (3 moles/l.) or benzoic acid (4 mmoles/l.) is added to anhydrous dimethylformamide or acetonitrile.

Thus the behaviour of carbonyl compounds in tetraethylammonium iodide solutions reported here (the existence of two waves, the wave heights and slopes, the constancy of behaviour with change of concentrations, and the formation of highly coloured ions during electrolysis) is consistent with the view that reduction takes place by two one-electron steps, the rate of addition of protons (or other ions) to the product of the first step being slow. Of course, in pure dry dimethylformamide only behaviour of type (*a*) would be possible. Since the results indicate that the rate of proton addition is low enough not to influence behaviour, the presence of a little water appears not to be significant. This

* The authors are indebted to a Referee for drawing attention to this possibility.

† The distinction between the significance of the values of n derived from the wave height and the slope is not always made clear in the literature; the first refers to the overall chemical change, the second refers to the mechanism of the potential-determining step.

[10] Coggan and Given, unpublished work.

conclusion is confirmed by the fact that the half-wave potentials were mostly not concentration-dependent, as one would expect them to be if uptake of protons from water were an important step; moreover, addition of 1% of water (550 mM) to 0·566 mM-anthraquinone in dimethylformamide containing less than 0·02% of water caused no significant change in the first half-wave potential of either diffusion current constant; the half-wave potential of the second wave became about 0·03 v less negative. The effect of adding acetic anhydride to a solution of a carbonyl compound before polarographic reduction parallels the effect of proton donors on the reduction of hydrocarbons, that is, the rate of removal of the mononegative ion by reaction becomes greater than its rate of diffusion from the electrode surface; in this case the reaction is not proton-addition but $RO' + Ac_2O \longrightarrow ROAc + OAc'$.

The product of addition of two electrons to a quinone is the quinol di-ion. The strong red colour of the anthraquinone solution during controlled potential electrolysis and its immediate discharge on the addition of acetic anhydride indicate that the di-ion remains stable, as the tetraethylammonium salt. The stationary-state analysis of Hoijtink *et al.*[5] shows two interesting consequences of the fact that, in the reduction of hydrocarbons in dioxan–water, protons are supplied to the *di*-negative ions from the water in the solvent, which is unbuffered: the second half-wave potential should be concentration-dependent, and logarithmic analysis of the wave should give a line of slope 0·084, not 0·059, at 25°. These predictions are found correct in the behaviour of hydrocarbons, but in the reduction of carbonyl compounds in dimethylformamide, where the di-negative ions are removed from the electrochemical equilibrium by a different process, the slope of the wave is indeed about 0·084, but its half-wave potential does not appear to be concentration-dependent for most of the substances within the concentration range studied. It is not easy to explain these facts.

In the reduction of ketones the di-negative ion has the structure $R_2C^-–O^-$, which may remain as a stable entity.[11] However if this captured a proton by reaction with the solvent (or the water contained in it), then the alkoxide ion, $R_2CH–O^-$, would undoubtedly be stable. Wawzonek *et al.*[1] showed that in the reduction of hydrocarbons in dimethylformamide and acetonitrile the di-negative ions do indeed abstract protons from the solvent, the negative solvent ion then decomposing or polymerizing.

The third wave given by xanthone appears to correspond to the addition of two further electrons, this time to the aromatic system. Purpurogallin also gave a third wave in very dilute solution, but this was small and perhaps was an adsorption post-wave; colchicine and colchiceine, which are structurally related to it, give small adsorption waves in aqueous buffer solution.[12]

No explanation can yet be given for the various peculiarities of behaviour in lithium chloride solutions. Some of the behaviour of 1 : 4-dihydroxyanthraquinone is consistent with the view that the third wave is due to adsorption of the quinone. However it should be borne in mind that this compound contains a hydroxyl group in the *peri*-position and proton transfer from this to the mononegative ion would be simple (this is also true of purpurogallin). The setting up of a tautomeric equilibrium of this kind would clearly interfere with the reduction process. The lithium ion can also form chelate complexes, whereas the tetraethylammonium ion cannot.

The authors are indebted to Mr. S. Marinkowič for some of the experimental work in this and the following paper. This paper and the two following are published by permission of this Association.

British Coal Utilisation Research Association,
Leatherhead, Surrey. [*Received, April 12th,* 1957.]

[11] Rausch, McEwen, and Kleinberg, *J. Amer. Chem. Soc.*, 1954, **76**, 3622.
[12] Brdicka, *Časopis Českého Lékárnictva*, 1945, **58**, 37.

548. *Polarographic Reduction of Carbonyl Groups in Solvent Extracts of Coals.*

By P. H. Given and J. M. Schoen.

Solvent extracts of coals in dimethylformamide solutions give distinct reduction waves in the range −0·4 to −0·7 v against the mercury pool owing to the presence of quinones. The height of the waves indicates that not all the molecules in these materials are quinones; some preferential extraction of the non-quinonoid substances is effected by certain solvents, but the effect in not marked. There are indications that the quinones present in different coals have similar structures.

All coals contain combined oxygen; in coals of carbon content up to 90% much of this [1, 2, 3] is in the form of phenolic hydroxyl; the intensity of the band at 1600 cm.$^{-1}$ in the spectra of coals is suggested to be due in part to quinone groups chelated to hydroxyl.[1] It was thought that reduction at the dropping-mercury electrode might provide an independent means of detecting and estimating quinone and other forms of carbonyl groups in the material extracted from coals by organic liquids. This possibility has been investigated, with the results reported here. Dimethylformamide, in which the polarographic behaviour of a number of aromatic carbonyl compounds was available for comparison,[4] was used as solvent. The proportion of coal extracted by the various solvents was not large (Tables 2 and 3). However, there are reasons (based, for example, on comparison of the infrared spectra of coals with the spectra of extracts of them [5]) for supposing that the soluble material does not differ essentially from the insoluble in basic chemical structure, so knowledge of the nature of the extract is relevant to the study of coals themselves.

Experimental

The apparatus, procedure, solvent, and electrolytes were as described previously.[4] Solvent extracts of four coals (Table 1) were studied; they were prepared as follows: the solvent and dried powdered coal (100 g. of coal to 1 l. of solvent) were irradiated with 25 kc./sec. ultrasonic

Table 1. *Analyses (%, w/w) of the coals (dry and ash-free).*

Coal	C	H	N	S	O (by diff.)
DO	77·8	5·3	1·2	2·6	13·1
DIII	81·1	5·2	1·8	1·6	10·3
DIX	86·1	5·3	2·2	0·7	5·7
DXIII	89·2	5·0	1·4	0·7	3·7

radiation (electrical power input 500—800 w) for 10 min. The insoluble residue, after filtration, was further extracted by heating with fresh solvent at 100° (or the b. p. of the solvent if lower) for 1 hr. The combined filtrates were either added directly to the supporting electrolyte solution or were evaporated to dryness in nitrogen at or below 100°. The ethylenediamine extract of the coal DIII, however, was prepared by shaking the powdered coal at room temperature for ½ hr. with solvent in a vessel provided with a porous-glass filter. After withdrawal of the liquid the residue was shaken with more solvent. The combined filtrates were diluted with much water, and hydrochloric acid was added to bring the pH to 3—4. The precipitate was thoroughly washed, then dried. The analyses of the products were similar to those of the original coals; they indicated in some cases a small retention of solvent but after allowance for this the extracts still appeared to contain somewhat more hydrogen and correspondingly less carbon (for typical figures see refs. 1, 2, 6, and 7).

[1] Wyss and Brown, *Chem. and Ind.*, 1955, 1118.
[2] Wyss, *ibid.*, 1956, 1095.
[3] Blom, Edelhausen, and van Krevelen, *Fuel*, 1957, **36**, 135.
[4] Given, Peover, and Schoen, preceding paper.
[5] Brown, *Fuel*, in the press.
[7] Rybicka, *Fuel*, in the press.
[6] Dryden, *Fuel*, 1952, **31**, 176.

Results.—The polarographic behaviour of solvent extracts of one coal (DIII) was studied; the extracting solvent was removed and the residue taken up in dimethylformamide (see Table 2). The term A' is $i_d/(c'm^{\frac{2}{3}}t^{\frac{1}{6}})$ where i_d is the diffusion current (μA), c' the concentration

TABLE 2. *Solvent extracts of coal DIII in dimethylformamide.*

Extracting solvent	Extract (% w/w of dry coal)	Concn. range (%)	$-E_{\frac{1}{2}}$ (v)	A'
Ethylenediamine	10	0·05—0·135	0·61	3·8
Butanone *	2	0·1	0·59	1·55
Acetone	3	0·1—0·17	0·57	1·4

* The coal had previously been extracted with acetone.

(% w/v), m the mass (mg.) of mercury flowing per sec., and t the drop-time (sec.). Also, a series of pyridine and dimethylformamide extracts of 4 coals were studied, without removal of the original solvent: the extract was so added to the base solution that the concentration of the

FIG. 1. *Polarograms in lithium chloride–dimethylformamide of* (*a*) 12 : 12′-*dimethoxydibenzanthrone and* (*b*) *ethylenediamine extract of coal DIII.*

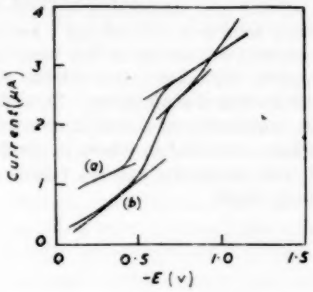
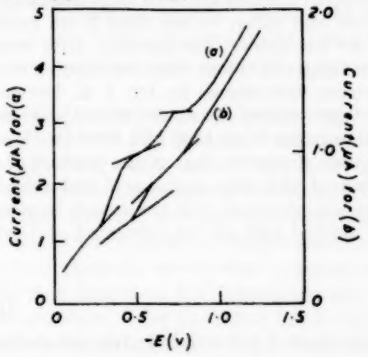


FIG. 2. *Polarograms in lithium chloride–dimethylformamide of pyridine extracts of coals* (*a*) *DIII and* (*b*) *DO.*



mixture was 0·05—0·2% in coal (see Table 3) and did not exceed 20% in pyridine. Pyridine itself gave no waves in the range of voltage studied, but it did influence the polarographic behaviour of the coals. Half-wave potentials are referred to the mercury pool, and all the results quoted were obtained with 1·0N-lithium chloride as supporting electrolyte. A few of the materials were also studied in 0·1N-tetraethylammonium iodide; the results were very similar, except that diffusion currents were higher.

TABLE 3. *Solvent extracts of four coals in dimethylformamide.*

Coal	Extracting solvent	Extract (% w/w of dry coal)	Concn. range (%)	$-E_{\frac{1}{2}}'$ (v)	$-E_{\frac{1}{2}}''$ (v)	A'
DO	Pyridine	10	0·05—0·1	N	0·57	2·9
	Dimethylformamide	10	0·094	N	N	—
DIII	Pyridine	10·5	0·08—0·16	0·36	0·67	3·5
	Dimethylformamide	3·7	0·12	N	0·67	1·8
DIX	Pyridine	12·5	0·05—0·11	N	0·67	2·2
	Dimethylformamide	9·9	0·08—0·17	N	0·68	1·4
DXIII	Pyridine	2·7	0·05—0·12	0·42	0·70	4·1

$E_{\frac{1}{2}}'$ and $E_{\frac{1}{2}}''$ are first and second waves respectively; N = no wave.

Polarograms of all the solvent extracts of coals showed considerable increases in current as the applied voltage increased in the range −0·2 to −1 v, and most of them showed distinct but not well-defined waves between −0·3 and −0·7 v (see examples in Figs. 1 and 2) which shifted slightly to more negative potentials with increasing concentration. The waves were

difficult to read (the method recommended by the makers of the instrument [9] was adopted as a standard procedure) and the reproducibility of diffusion currents was not good.

The half-wave potentials in the Tables all lie within a narrow range; all the coal extracts show a wave at $-0{\cdot}63 \pm 0{\cdot}07$ v, and two of them a second wave at about $-0{\cdot}4$ v. The effect of the presence of some pyridine in the base solution is not consistent: with coal DO, one wave is seen in the presence of pyridine and none in its absence, with DIII a second wave appears, and with DIX no effect is observed. These effects may be due to pyridine's being a base. If a little piperidine was added to the dimethylformamide solution of the extract of DIII, the behaviour became the same as that of the solution containing pyridine. There is no reason to suppose that pyridine and dimethylformamide extract essentially different materials from the coals.

Plots of $\log i/(i_d - i)$ against the voltage E_{de} were made from a number of the polarograms (i is the current at any potential E_{de} of the dropping electrode). Satisfactory straight lines were obtained, whose slopes corresponded approximately to $n = 1$ [*e.g.*, 0·90, 0·93, 0·98, 1·0 (3 times), 1·2 (twice), 1·3].

An electrolytic reduction of a dimethylformamide extract of the coal DIII at a controlled potential of $-1{\cdot}5$ v (*vs.* saturated aqueous calomel electrode) was carried out by M. Peover in a cell similar to that described by Lingane, Swain, and Fields.[10] The solvent extract was dissolved in dimethylformamide with tetraethylammonium iodide as supporting electrolyte. When the current had fallen to less than 1 mA excess of acetic anhydride was added and the solution left for two days. The product, after removal of the solvent and supporting electrolyte, was much lighter in colour than the starting material and easily soluble in chloroform. Its infrared spectrum (determined by Dr. J. K. Brown) showed a marked weakening of the band at 1600 cm.$^{-1}$ (previously associated with the presence of quinones; see below), two intense phenolic acetate bands near 1200 and 1760 cm.$^{-1}$, and very weak hydroxyl absorption. This spectrum was very similar to that of the product of the reductive acetylation of a similar extract of the same coal with zinc, acetic acid and anhydride, and sodium acetate [1] in whose polarogram no wave was observed, and the steady increase in current with increasing applied voltage, which was marked with all the untreated coal extracts, was only slight.

Discussion

Controlled potential electrolysis makes it clear that the polarographic waves shown by solvent extracts of coals in the range $-0{\cdot}4$ to $-0{\cdot}7$ v (against the mercury pool) are due to the presence of carbonyl groups. Comparison of the half-wave potentials observed with values for known carbonyl compounds studied under the same conditions [4] shows that the carbonyl groups in the solvent extracts of coals must be strongly conjugated to aromatic systems. Of the known compounds studied, only quinones have half-wave potentials as low as those found for the coal extracts. We therefore conclude that these materials contain quinones, as did Wyss and Brown [1] from a comparison of the infrared spectra of solvent extracts of a coal with the spectra of the products of reductive acetylation. A strong band close to 1600 cm.$^{-1}$ is prominent in the spectra of all coals and their solvent extracts,[11] the assignment of which to a functional group is equivocal on spectroscopic grounds alone. Wyss and Brown,[1] however, showed that its intensity is markedly weakened if solvent extracts of a coal are reductively acetylated, from which they deduced that the assignment to quinonoid carbonyl strongly chelated to hydroxyl is correct (the weak benzene-ring skeletal vibration at the same frequency would also contribute). This concord between the different methods establishes the presence of quinone groups in coals. This band is of very nearly constant frequency for all coals, and its intensity decreases only slightly with increasing carbon content up to about 93% of carbon. This constancy indicates that the carbonyl groups have a closely similar molecular environment in all

[9] Anon., Polarography with Tinsley Polarographs, Instruction Book No. ETP 460, Evershed and Vignoles Ltd., London, 1955.
[10] Lingane, Swain, and Fields, *J. Amer. Chem. Soc.*, 1943, **65**, 1348.
[11] Brown and Hirsch, *Nature*, 1955, **175**, 229.

coals and is matched by the narrow range of voltage within which lie the half-wave potentials of extracts of four coals. Although a possible explanation of the fact that the waves are superimposed on a steadily rising diffusion current is that a series of quinones are present in coals, having a range of half-wave potentials, and that the waves observed merely represent preferred values of the potentials, yet two pure compounds, 12 : 12′-dimethoxydibenzanthrone (see Fig. 1) and 1 : 2 : 5 : 8-tetrahydroxyanthraquinone, also give poorly defined waves superimposed on a steadily rising current, though the effect is less marked.[4]

Comparison of Tables 2 and 3 shows that there is some variation in the half-wave potentials and the diffusion currents of the series of solvent extracts of the coal DIII with the fraction of coal extracted. Some fractionation is evidently effected by extraction with different solvents, but not into materials of radically different structure. The behaviour of the ethylenediamine extract is of interest because the heat of immersion of coal DIII in it is so high (65 cal./g. at 25°; cf. 25 cal./g. for methanol [12]) that specific interaction must be suspected. Moreover an ethylenediamine extract, precipitated with hydrochloric acid, retains a small amount of solvent even after prolonged washing, as is shown by the higher nitrogen content of the dried extract (3·4%) in the material prepared for the present work than in that of the original coal (2·0%). The diamine possibly reacts with carbonyl groups in the coal giving a glyoxaline ring or other heterocyclic system. But as the only type of carbonyl group in coals for which there is evidence is the quinonoid, and if they had so reacted the polarographic behaviour could hardly have been that observed, some other explanation of the interaction must be sought.

The diffusion current constants, $i_d/(cm^{\frac{2}{3}}t^{\frac{1}{6}})$, of all the quinones of known structure studied in lithium chloride–dimethylformamide were abnormally low and had about the value expected for a one-electron addition, although two waves were observed in most cases;[4] the wave heights were more normal in tetraethylammonium iodide solutions. Where a coal extract has been studied in both lithium chloride and tetraethylammonium iodide solutions, the diffusion current was lower in the former. A more serious uncertainty in the diffusion current constants arises from the fact that the waves were superimposed on a steadily rising current. If one takes merely the height of the waves one may be neglecting part of the current due to reduction of quinones. On the other hand the rise in current between, say, 0 and −1 v may be not wholly diffusion current. One cannot therefore estimate quinone contents accurately from diffusion current constants by means of the Ilković equation. However it appears, from diffusion coefficients of the coal extracts in dimethylformamide, measured by Coggan and Given,[13] and the polarographic wave heights, that the pyridine extracts contain 2 g.-atoms of oxygen as quinone per 3000—5000 g. If one takes instead the rise in current between −0·1 and −1 v these weights of coal are about halved. Since the molecular weights of the materials, estimated from the diffusion coefficients, are about 2000 for the extract of coal DO and 600—900 for the others, it appears that not all the molecules in the materials are quinones. One might therefore expect quinones or non-quinones to be preferentially extracted from coals by some solvents. Some such effect can be observed in the varying diffusion current constants of the extracts of coal DIII (see Tables 2 and 3; the term $D^{\frac{1}{2}}$ appearing in the Ilković equation does not differ greatly for these extracts).

For comparison, we mention some other estimates of the quinone contents of coals and their solvent extracts. Wyss and Brown estimated a figure of 2 g.-atoms of oxygen as quinone per 6400 g. for the acetone extract of coal DIII. Peover, from the quantity of electricity passed in electrolytic reduction of another extract of the same coal (see above), obtained a figure of 1300 g. Blom *et al.*[3] attempted to determine carbonyl groups in coals by oximation. They found that the uptake of hydroxylamine, calculated from the difference in nitrogen content of the oximated product before and after hydrolysis, was much greater (3—16 times) than the amount liberated from the product by hydrolysis;

[12] Bangham and Dryden, *Fuel*, 1950, **29**, 291.
[13] Coggan and Given, unpublished measurements.

the latter was determined by reduction with titanous chloride and estimation of the ammonia produced. Their method did not give satisfactory results with a number of known compounds. They report carbonyl contents, which they regard as minimum figures, corresponding to 2 g.-atoms of oxygen as carbonyl per 5300—16,000 molecular-weight units, depending on the carbon content of the coal.

We thank Mr. M. Peover for the results of the controlled-potential electrolysis, and Dr. J. K. Brown for the infrared spectra.

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549. *Polarography of Conjugated Systems in Dimethylformamide.*

By P. H. GIVEN.

The polarographic reduction of naphthalene, anthracene, phenanthrene, pyrene, and coronene at the dropping-mercury electrode in dimethylformamide suggests that the mechanism is that previously established [1] for the reduction of aromatic systems in dioxan–water mixtures. Pyridine and quinoline give waves indicating reduction by a similar mechanism. The reduction of the aromatic systems in 2-naphthol, 2-methoxynaphthalene, anthraquinone, and 9 : 10-diacetoxyanthracene provides examples of the behaviour of oxygen-containing derivatives; all three substances showed waves suggesting that the aromatic systems were being reduced.

THE reduction of polycyclic aromatic hydrocarbons at the dropping-mercury electrode has been studied in dioxan–water,[1-3] acetonitrile,[4] and 2-methoxyethanol,[5] and its mechanism discussed.[1,4] The results are of theoretical interest, since half-wave potentials have been taken as measures of the energy states of the hydrocarbon molecules.[6] The experimental data have now been extended to some polycyclic aromatic hydrocarbons in dimethylformamide, and also to some oxygenated derivatives and two nitrogen heterocycles. Although the polarographic reduction of aromatic bases in an aprotic solvent and of the aromatic systems in oxygenated derivatives has not been reported previously, dimethylformamide was used for the polarography of some hydrocarbons related to stilbene.[4]

EXPERIMENTAL

The supporting electrolyte, 0·1M-tetraethylammonium iodide in dimethylformamide, apparatus, and procedure were as previously described.[7] Naphthalene, anthracene, 2-naphthol, anthraquinone, pyridine, and quinoline were " pure " commercial samples, used as received. Phenanthrene was treated (by Coggan) with sodium and distilled. Pyrene and coronene were purified samples kindly supplied by Dr. N. Sheppard. 9 : 10-Diacetoxyanthracene, prepared by reductive acetylation of anthraquinone with zinc dust, sodium acetate, and acetic anhydride,[7a] crystallized from acetic acid and had m. p. 265° (lit., 261°); polarography showed the absence of anthraquinone.

The reported potentials are all referred to the mercury pool anode, which is stable and reproducible under our conditions.[7] The diffusion current constants $A = i_d/(cm^{\frac{2}{3}}t^{\frac{1}{6}})$ (see ref. 8) were corrected for the change of drop-time with applied potential as described by Hoijtink *et al.*[1]

[1] Hoijtink, van Schooten, de Boer, and Aalbersberg, *Rec. Trav. chim.*, 1954, **73**, 355.
[2] Laitinen and Wawzonek, *J. Amer. Chem. Soc.*, 1942, **64**, 1765, 2365.
[3] Hoijtink and van Schooten, *Rec. Trav. chim.*, 1952, **71**, 1089.
[4] Wawzonek, Blaha, Berkey, and Runner, *J. Electrochem. Soc.*, 1955, **102**, 235.
[5] Bergman, *Trans. Faraday Soc.*, (*a*) 1954, **50**, 829; (*b*) 1956, **52**, 690.
[6] Hoijtink, de Boer, and van Schooten, *Rec. Trav. chim.*, 1955, **74**, 1525.
[7] Given, Peover, and Schoen, *J.*, 1958, 2674.
[7a] Calderbank, Johnson, and Todd, *J.*, 1954, 1285.

Results.—The experimental results are collected in the Table.

Substance	Concn. range (mmole/l.)	$-E_{\frac{1}{2}}$ (v)	A Partial	A Total	n *	$-E_{\frac{1}{2}}$ in Bu_4NI in 90% dioxan–water (v) †
Naphthalene	0·2 —1·3	1·99	1·85	1·85	1	2·04
Anthracene	0·25—1·5	1·41, 1·88	2·2, 1·9	4·1	2	1·42, 1·88
Phenanthrene	0·5 —1·9	1·93	2·1	2·1	1	1·94
Pyrene	0·5 —2·0	1·56, 2·03	2·0, 1·3	3·3	2	1·54, 2·01
Coronene	0·2 —0·8	1·53, 2·03	1·9, 4·6	6·5	4	1·49, 1·88
2-Naphthol	0·5 —1·5	1·99	1·25	1·25	?	—
2-Methoxynaphthalene	0·4 —1·3	2·03	2·05	2·05	1	—
Anthraquinone	0·2 —1·1	2·15	— ‡	—	—	—
9 : 10-Diacetoxyanthracene	0·3 —1·3	1·19, 1·65 2·02, 2·12	1·5, 2·95, $i_3 + i_4 = 3·45$	7·90	4	—
Pyridine	0·7 —1·3	2·01	4·55	4·55	2	—
Quinoline	0·25—0·9	1·53	3·75	3·75	2	—

* For overall change, calculated by means of Ilkovič equation; see below. † Results due to Hoijtink *et al.*,[1] for comparison. ‡ The waves due to reduction of the quinone groups are not included; a reliable wave-height cannot be given for reasons stated in the text.

The plot of $E_{d.e.}$ against log $i/(i_d - i)$ (see preceding paper) for the first wave given by each substance was a good straight line; in cases where two or more waves were observed, the slope of this line was approximately 0·06 (values in the range 0·055—0·066 were obtained). Where a substance gave only one wave, the slope was higher (0·07—0·09). For the second waves, where they were observed, the slope was always greater than 0·059 (usually about 0·08). Bergman [5] has estimated the diffusion coefficients of a number of hydrocarbons by means of the Stokes–Einstein equation, suitably corrected, and concludes that for a molecule of the size of anthracene a diffusion current constant of about 3·0 corresponds to a two-electron reduction, and for molecules the size of pentacene the value is nearer 2·0. Approximate diffusion coefficients for anthracene, pyrene, and coronene in dimethylformamide were obtained by Coggan and Given; [6] their use in the Ilkovič equation gives the values of n shown in the Table and suggests that the values of the diffusion current constant corresponding to Bergman's figures of 3 and 2 are higher for dimethylformamide (about 4 and 3), which is consistent with its lower viscosity than that of Cellosolve. The other values of n in the Table were obtained by use of the above approximate figures for the diffusion current constant per two electrons added. The half-wave potentials of none of the substances studied changed with concentration in the range stated.

The wave given by anthraquinone at −2·15 v was not clearly resolved from that of the decomposition of the supporting electrolyte and was anomalous in certain respects. The diffusion current " constant " decreased from 2·65 at 0·236 mM (*i.e.*, $n \approx 1·3$) to 1·65 at 1·09 mM. If 0·1—0·4% of water (about 50—200 mM) was added the diffusion current constant increased markedly and became more nearly independent of the concentration of anthraquinone (about 4·0 at water : anthraquinone mole ratio of 200, and about 5·2 when the ratio was 400). At any given concentration of anthraquinone (with no added water) the diffusion current gave an approximately straight-line plot against the height of the mercury reservoir (corrected for back pressure).

The addition of water (0·2—1·0%) to millimolar solutions of anthracene or pyrene made the half-wave potentials of the second waves less negative by 0·03—0·04 v and in the case of pyrene increased the height of the first wave by about 10%.

Discussion

The half-wave potentials of the five hydrocarbons studied in dimethylformamide are strikingly similar to the corresponding values measured in 96% dioxan–water, if all potentials are referred to the mercury pool. The agreement is still noteworthy, though less striking, if all potentials are referred to the aqueous calomel electrode. The same five compounds have also been studied in 2-ethoxyethanol,[5] and anthracene in acetonitrile as

[6] Coggan and Given, unpublished work.

well;[4] the potentials are on the whole similar to those in the Table. The anode potentials in the four media mentioned differ much less among themselves than any one of them differs from the calomel potential. Theoretically one might expect not only the anode potentials but also the solvation energies of the ions to differ in different solvents; moreover in any comparison of potentials in different solvents a liquid junction potential is necessarily implied. The similarities observed are therefore unexpected; they are too numerous to be dismissed as coincidence, and must be significant.

The other characteristics of polarographic reduction of hydrocarbons in dimethylformamide (number of waves, heights and slopes of waves) also resemble those observed in other solvents, particularly 96% dioxan–water. For anthracene, pyrene, coronene, and 9 : 10-diacetoxyanthracene these characteristics are those expected, on the analysis of mechanism by Hoijtink *et al.*,[1] for reductions by one-electron potential-determining steps in which proton addition to the intermediate mononegative ions is slow (cf. the reduction of quinones [7]); in the case of coronene, the dihydro-derivative evidently has a higher electron affinity than coronene itself, since two further electrons are added with no decrease in potential (pyrene behaves similarly in 75% dioxan–water [1]). All the other substances in the Table show one wave only. According to the mechanism of Hoijtink *et al.*[1] one wave is found when the rate of addition of protons to the mononegative ion is fast compared with the diffusion of the ion from the electrode surface; in these circumstances the monohydro-radical at once adds a second electron without change in potential, since all such hydrocarbon radicals necessarily have higher electron affinities than their parent hydrocarbons.[1] Logarithmic analysis of the single wave should give a line of slope about 0·08—which in this context indicates a one-electron potential-determining step—but the wave-height should correspond to the addition of two electrons. The slopes of the single waves observed in dimethylformamide solutions are in agreement with these conclusions, but their heights are in many cases surprisingly low.

The completion of the reduction process requires the addition of protons to the negative ions. In our dimethylformamide there are two possible sources of protons, namely, water as impurity (0·02—0·1%; *ca.* 10—50 mM) or the solvent. Water is probably unimportant as a proton donor (except with anthraquinone): deliberate addition of up to 550 mmoles/l. had little effect on the polarography of anthracene or pyrene, although it had some effect on that of anthracene in acetonitrile, but only when 5% (about 3 moles/l.) or more is present. Wawzonek *et al.*[4] showed that although dimethylformamide does not release protons by ionization, hydrocarbon ions can abstract protons from it in a bimolecular reaction: the remaining ion $CO{\cdot}NMe_2^-$ then decomposes. We therefore conclude that the solvent is usually the effective source of protons. The case of anthraquinone is dealt with below. In aqueous solution pyridine and quinoline give [9] catalytic hydrogen waves as well as reduction waves and the polarographic behaviour depends strongly on the supporing electrolyte and pH. As they could not give such waves in an aprotic solvent, their behaviour in dimethylformamide is consistent with the view that the aromatic ring is being reduced.

It is now accepted that the half-wave potential for a hydrocarbon measures the energy needed to place one or more electrons in the lowest unoccupied molecular orbital.[5,6,10] Thus electron affinities have been calculated from half-wave potentials [6] by an algebraic method that obviates the necessity of knowing the potentials on the hydrogen scale (see also Matsen [11]) and compared with values calculated from molecular-orbital theory. Bergman [5] has found that when the half-wave potentials of aromatic hydrocarbons are plotted against the frequency ($cm.^{-1}$) of the first *p*-band (in Clar's nomenclature [12]) in the absorption spectrum, the points fall on sets of straight lines of similar slope but differing

[9] Kolthoff and Lingane, "Polarography," Interscience, New York, 2nd Edn., 1952, pp. 813, 818.
[10] Maccoll, *Nature*, 1949, **163**, 178.
[11] Matsen, *J. Chem. Phys.*, 1956, **24**, 602.
[12] Clar, "Aromatische Kohlenwasserstoffe," Springer-Verlag, Berlin, 2nd Edn., 1952.

intercept according to the type of aromatic system present. The absorption bands in the spectra of pyridine and quinoline have not been identified as *p*, α and β, nor is it clear whether or how this system of classification is applicable to heterocyclic compounds. However, if the frequency of the first band in the spectra of pyridine and quinoline (38,250 and 32,000 $cm.^{-1}$ respectively) is plotted against half-wave potential, the line joining the two points is nearly parallel to Bergman's line for the cata-condensed hydrocarbons (*i.e.*, hydrocarbons with not more than two carbon atoms common to any pair of benzene rings), but of higher intercept on the frequency axis.

No systematic study of the reduction of the aromatic system in substituted derivatives has been made. Provided that the substituent is not itself reducible at the dropping-mercury electrode or capable of giving a catalytic hydrogen wave, the polarographic behaviour should not be much changed by substitution: one might expect a small decrease in half-wave potential to correspond with the small bathochromic shift usually observed in the ultraviolet spectrum (introduction of a methyl group into naphthalene changes the half-wave potential by −0·25 v [13]). The figures in the Table for naphthalene and its derivatives support this view. (Monocyclic phenols do not give hydrogen discharge or reduction waves in dimethylformamide.) If the substituent is reducible, then any further waves observed must represent reduction of the first reduction product. Thus anthraquinone gave a wave at −2·15 v; this presumably represents addition of one or more electrons to the conjugated system in 9 : 10-dihydroxyanthracene or its di-ion. The low values of the diffusion current constant for this wave and their decrease with increasing concentration may be associated with the difficulty of adding further electrons to an ion already doubly-negatively charged. The marked increase in wave height on the addition of water is in accord with this suggestion, since one might expect water partly to hydrolyse the tetraethylammonium salt of 9 : 10-dihydroxyanthracene. The polarography of 9 : 10-dihydroxyanthracene has not been studied, since its ready oxidation makes it difficult to obtain and handle. 9 : 10-Diacetoxyanthracene shows different behaviour from anthraquinone; it apparently undergoes a four-electron reduction. 1-Hydroxy- and 1 : 4-dihydroxy-anthraquinone did not show any wave between the quinone waves and the decomposition potential of the base electrolyte (−2·25 v). A proper understanding of the behaviour of substituted derivatives clearly requires further work.

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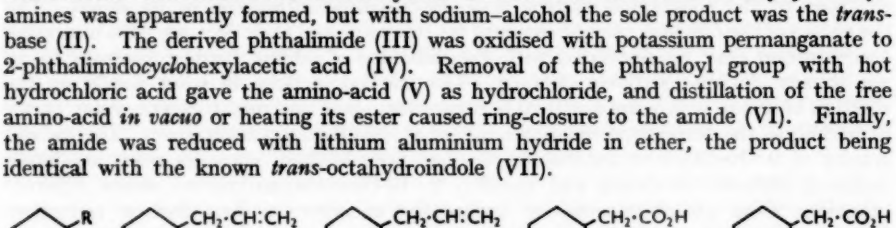
[13] Hoijtink and van Schooten, *Rec. Trav. chim.*, **1953**, **72**, 691.

550. *Synthetic and Stereochemical Investigations of Reduced Cyclic Bases. Part VI.* A New Synthesis of* trans-*Octahydroindole and a Re-investigation of its Hofmann Methylation Products.*

By H. Booth and F. E. King.

An improved synthesis of *trans*-octahydroindole has been devised starting from 2-allyl*cyclo*hexanone, and with the greater availability of this amine the decomposition of its *N*-methyl methohydroxide has been re-investigated. The newer experiments have apparently given a more readily purified methine and revised melting points of salts of its dihydro-derivative correspond with those of *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine.

The synthesis of *cis*- and *trans*-octahydroindole described in Part III [1] requires 2-2′-ethoxyethyl*cyclo*hexanone (I; R = ·CH_2·CH_2·OEt), the amino-group being introduced at the keto-position either mainly *cis* by the Leuckart reaction, or wholly *trans* by sodium–alcohol reduction of the oxime. The preparation of the ketone (I; R = ·CH_2·CH_2·OEt) is tedious and the route to *trans*-octahydroindole has been simplified by using the more easily obtainable 2-allyl*cyclo*hexanone [2] (I; R = ·CH_2·CH:CH_2). When the ketoxime was reduced with lithium aluminium hydride a mixture of the isomeric 2-allyl*cyclo*hexylamines was apparently formed, but with sodium–alcohol the sole product was the *trans*-base (II). The derived phthalimide (III) was oxidised with potassium permanganate to 2-phthalimido*cyclo*hexylacetic acid (IV). Removal of the phthaloyl group with hot hydrochloric acid gave the amino-acid (V) as hydrochloride, and distillation of the free amino-acid *in vacuo* or heating its ester caused ring-closure to the amide (VI). Finally, the amide was reduced with lithium aluminium hydride in ether, the product being identical with the known *trans*-octahydroindole (VII).



An alternative synthesis of the amino-acid (V) was explored which began with 1-*cyclo*hex-1′-enylpyrrolidine from which ethyl 2-oxo*cyclo*hexylacetate (VIII) was formed by treatment with ethyl bromoacetate.[3] However, hydrogenation of the ketoxime in alcoholic ammonia with Raney nickel appeared not to be stereospecific since after hydrolysis with hydrochloric acid the product consisted of the mixed amino-acid salts, and repeated crystallisation was necessary to obtain the pure *trans*-hydrochloride. The method was therefore not pursued.

The larger amounts of *trans*-octahydroindole obtainable by the improved synthesis

* Part V, Booth, King, and Parrick, *J.*, 1958, 2302.

[1] King, Bovey, Mason, and Whitehead, *J.*, 1953, 250.

[2] *Org. Synth.*, Coll. Vol. III, p. 44 (1955).

[3] Stork, Terrell, and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1954, **76**, 2029.

enabled a more precise examination of the decomposition of its *N*-methyl methohydroxide to be made. Former experiments [1] gave a methine which was believed to have a rearranged carbon skeleton since its dihydro-derivative appeared to differ from both products to be expected from normal degradation. The earlier limited specimens of the dihydro-derivative were characterised in the form of the picrate (m. p. 106°), picrolonate (160°), and methiodide [221° (decomp.)]. With the larger quantities now forthcoming, melting points of the derivatives were picrate 123—124°, picrolonate 172—173°, and methiodide 221° (decomp.), indicating higher purity of the degradation product, due probably to improved quality of the octahydroindole.

The melting points of the new specimens of the three derivatives resemble closely (as do other constants, *e.g.*, refractive index and m. p. of the hydriodide) those of *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine [1,4] (IX), so that the product of the Hofmann change is *trans*-*NN*-dimethyl-2-vinyl*cyclo*hexylamine. It is evident, therefore, that scission of the $N-C_{(2)}$ bond has taken place, whereas in the decomposition of *cis*-octahydro-1-methylindole methohydroxide it is the $N-C_{(8)}$ bond which is severed. This contrasting behaviour of the two isomers is not unexpected in view of the conformational features mentioned in Part IV [5] although it is now clear that the consequences for the *trans*-methohydroxide were there incorrectly interpreted.

Ring-scission of the *trans*-isomer differs from that of the *cis*-compound also in the formation from the *trans*-methohydroxide of a by-product $C_{20}H_{40}ON_2$. This has already been recognised as an ether by hydrolysis with hydrobromic acid to a bromo-amine salt, $C_{20}H_{20}NBr,HBr$, and a tentative constitution has been assigned to it.[5] With hydriodic acid the ether gives the presumably analogous iodo-compound which is reduced by zinc and acetic acid to the foregoing *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine, thus disclosing the structure of the ether as (X). The formation of an ether of this type suggests that conditions are unfavourable for proton removal by hydroxyl ion attack at position 3, an essential feature of the Hofmann reaction. Here again conformational factors are probably involved since molecular models reveal that the requirement for easy elimination of the hydrogen at this position is lacking.

Experimental

trans-2-*Allyl*cyclo*hexylamine*.—2-Allyl*cyclo*hexanone [3] (60 g.) was converted by the usual procedure into the oxime (62 g., 93%), m. p. 71—72° (Cope, Hoyle, and Heyl [6] record m. p. 70—70·5°). The oxime (17 g.), in boiling ethanol (200 c.c.), was treated with sodium (50 g.) added in small pieces during 1·5 hr. After the mixture had been refluxed for a further 30 min., excess of sodium was removed by the addition of aqueous ethanol. The cooled solution was acidified with 15% hydrochloric acid, then evaporated to remove ethanol, and non-basic material was removed with ether. The aqueous solution was made alkaline and the liberated base was extracted with ether. trans-2-*Allyl*cyclo*hexylamine* (12·8 g., 83%) was thus isolated as a colourless oil, b. p. 69—70°/9 mm. The base, which was not itself analysed owing to its rapid conversion into carbonate on exposure to air, yielded the following derivatives: *picrate*, crystallising from ethanol in prisms, m. p. 178—179° (Found: C, 49·0; H, 5·8; N, 14·9. $C_{15}H_{20}O_7N_4$ requires C, 48·9; H, 5·5; N, 15·2%); *picrolonate*, needles, m. p. 217—218°, from ethanol (Found: C, 56·8; H, 6·2; N, 17·6. $C_{19}H_{28}O_5N_8$ requires C, 56·6; H, 6·2; N, 17·4%); *acetyl derivative*, crystallising from light petroleum (b. p. 60—80°) in needles, m. p. 107—108° (Found: C, 72·7; H, 10·4; N, 7·7. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·6; N, 7·7%); *benzoyl derivative*, crystallising from ethanol in needles, m. p. 137—138° (Found: C, 79·1; H, 8·8; N, 5·85. $C_{16}H_{21}ON$ requires C, 79·0; H, 8·7; N, 5·8%).

Treatment of the base (2·3 g.) with 40% aqueous formaldehyde (3 c.c.) and 90% formic acid (7 c.c.) for 2 hr. on a steam-bath, followed by ether-extraction of the basified solution, gave *trans*-2-allyl-*NN*-dimethyl*cyclo*hexylamine (2·4 g.). The tertiary base yielded a picrate

[4] King, Barltrop, and Walley, *J.*, 1945, 277.
[5] King and Booth, *J.*, 1954, 3798.
[6] Cope, Hoyle, and Heyl, *J. Amer. Chem. Soc.*, 1941, **63**, 1843.

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which crystallised from ethanol in prisms, m. p. 100—101° (Fujise [7] records 101—102°; Bailey, Haworth, and McKenna [8] record 100—101°).

Reduction of 2-Allylcyclohexanone Oxime with Lithium Aluminium Hydride.—The oxime (0·5 g.), in dry ether, was added to a solution of lithium aluminium hydride (0·5 g.) in dry ether. The mixture was refluxed for 2·5 hr. and worked up by ether-extraction of the basified mixture. The resulting oil, which was probably a mixture of *cis*- and *trans*-amines, was converted into the benzoyl derivative, m. p. 109—111°. Five recrystallisations from light petroleum (b. p. 60—80°) gave a poor yield of *trans*-1-allyl-2-benzamidocyclohexane, m. p. and mixed m. p. 137—138°.

N-(trans-2-*Allylcyclohexyl*)*phthalamic Acid.*—*trans*-2-Allylcyclohexylamine (5·8 g.), dry chloroform (50 c.c.), and phthalic anhydride (6·2 g.) were heated under reflux for 1 hr. The cooled mixture was extracted three times with sodium hydrogen carbonate solution and the combined extracts were acidified with dilute hydrochloric acid. The precipitate (7·5 g., 63%) was collected, dried, and crystallised from ethanol. N-(trans-2-*Allylcyclohexyl*)*phthalamic acid* was thus obtained in colourless needles, m. p. 161—162° (Found: C, 71·0; H, 7·2; N, 4·8. $C_{17}H_{21}O_3N$ requires C, 71·1; H, 7·4; N, 4·9%).

trans-1-*Allyl*-2-*phthalimidocyclohexane.*—(i) A solution of the above phthalamic acid (7·5 g.) in acetic anhydride (20 c.c.) was refluxed for 1 hr. and then poured into water. trans-1-*Allyl*-2-*phthalimidocyclohexane* (4·5 g., 63%) was recovered by filtration. Crystallisation from ethanol gave needles, m. p. 90—91·5° (Found: C, 75·9; H, 7·3; N, 5·35. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·2%). (ii) *trans*-2-Allylcyclohexylamine (12·8 g.), glacial acetic acid (75 c.c.), and phthalic anhydride (14 g.) were refluxed gently for 5½ hr. The hot mixture was poured into cold water (500 c.c.): an oil was produced which soon solidified. The crude imide was purified by suspending it in dilute sodium carbonate solution and filtering. The residue of *trans*-1-allyl-2-phthalimidocyclohexane (22·4 g., 90%), m. p. 85—87°, crystallised from ethanol in needles, m. p. 90—91·5°.

trans-2-*Phthalimidocyclohexylacetic Acid.*—Potassium permanganate (30 g.) was added during 2 days to a stirred solution of *trans*-1-allyl-2-phthalimidocyclohexane (15·2 g.) in pure dry acetone (600 c.c.). Finally the mixture was filtered and the residue was suspended in dilute sulphuric acid containing crushed ice. Sulphur dioxide was passed through the mixture until no more manganese dioxide remained, after which the solution was filtered. Crystallisation of the residue from aqueous methanol gave trans-2-*phthalimidocyclohexylacetic acid* (12·75 g., 79%), m. p. 172—173·5° (Found: C, 66·8; H, 6·2; N, 4·5. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0; N, 4·9%). The *methyl ester* crystallised from methanol in needles, m. p. 131—132° (Found: C, 67·8; H, 6·3; N, 4·9. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·7%). The *ethyl ester* crystallised from aqueous ethanol in needles, m. p. 67—68° (Found: C, 68·9; H, 6·4; N, 4·6. $C_{18}H_{21}O_4N$ requires C, 68·6; H, 6·7; N, 4·4%).

trans-2-*Acetamidocyclohexylacetic Acid.*—The oxidation of *trans*-1-acetamido-2-allylcyclohexane (7·2 g.) with potassium permanganate (21 g.) was carried out as described above for the corresponding phthalimido-compound. The resulting *acid* (5·6 g., 71%), m. p. 178—180°, was purified by crystallisation from water, from which it was obtained in needles, m. p. 184—185° (Found: C, 60·7; H, 8·63; N, 7·1. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·6; N, 7·0%).

trans-2-*Aminocyclohexylacetic Acid.*—*trans*-2-Phthalimidocyclohexylacetic acid (15 g.), concentrated hydrochloric acid (200 c.c.) and ethanol (50 c.c.) were heated under reflux for 48 hr. The solution was cooled in the ice-chest, filtered from phthalic acid, and extracted three times with ether. The residual aqueous phase was then evaporated under reduced pressure on a water-bath, giving trans-2-*aminocyclohexylacetic acid hydrochloride* (8·4 g., 83%). Crystallisation from methanol–ether gave needles, m. p. 216—217° (Found: C, 49·8; H, 8·1; N, 7·3; Cl, 18·7. $C_8H_{16}O_2NCl$ requires C, 49·6; H, 8·3; N, 7·2; Cl, 18·3%). The hydrochloride (20 g.) was shaken in the dark with a suspension in water (150 c.c.) of silver carbonate, freshly prepared from silver nitrate (30 g.) and sodium carbonate (10 g.). The mixture was left overnight and then filtered from silver chloride. The filtrate was treated with hydrogen sulphide, filtered from silver sulphide, and evaporated to dryness. Crystallisation of the residue from slightly aqueous methanol gave trans-2-*aminocyclohexylacetic acid monohydrate*, m. p. 221° (decomp.) (11·6 g., 64% from the hydrochloride) (Found: C, 54·8; H, 9·7; N, 8·2. $C_8H_{15}O_2N,H_2O$ requires C, 54·9; H, 9·8; N, 8·0. Found, after drying at 110°: C, 61·3;

[7] Fujise, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1928, **8**, 185.
[8] Bailey, Haworth, and McKenna, *J.*, 1954, 967.

H, 9·9. $C_8H_{15}O_2N$ requires C, 61·1; H, 9·6%). The *picrate*, prepared from the hydrochloride and aqueous sodium picrate, crystallised from water in prisms, m. p. 177—179° (Found: C, 43·8; H, 4·6; N, 14·3. $C_{14}H_{18}O_9N_4$ requires C, 43·5; H, 4·7; N, 14·5%). The *benzoyl derivative* crystallised from methanol in needles or prisms, m. p. 194—195° (Found: C, 68·7; H, 7·3. $C_{15}H_{19}O_2N$ requires C, 69·0; H, 7·3%). The prism form was converted into the needle form with slight softening, at about 180°.

Methyl trans-2-*Amino*cyclo*hexylacetate*.—The above amino-acid hydrochloride (18·9 g.) was dissolved in dry methanol (250 c.c.) containing hydrochloric acid (about 5% w/v) and heated under reflux for 12 hr. The solution was finally distilled to remove excess of methanol, cooled, and poured into saturated ice-cold potassium carbonate solution (100 c.c.) covered by a layer of ether (100 c.c.). After separation of the ether, the aqueous phase was extracted with further portions of ether (4 × 100 c.c.). Removal of the ether gave *methyl* trans-2-*amino*cyclo*hexylacetate* (12·1 g., 72%), b. p. 135—150° (bath-temp.)/10 mm. (Found: C, 63·4; H, 9·9. $C_9H_{17}O_2N$ requires C, 63·1; H, 10·0%). The amino-ester gave the following derivatives: *hydrochloride*, crystallising from methanol–ether in needles, m. p. 153—154° (Found: C, 52·0; H, 8·6. $C_9H_{18}O_2NCl$ requires C, 52·0 ; H, 8·7%); *picrate*, prepared from the hydrochloride and aqueous sodium picrate, and crystallising from aqueous methanol in needles, m. p. 114—116° (Found: C, 45·3; H, 5·0; N, 14·1. $C_{15}H_{20}O_9N_4$ requires C, 45·0; H, 5·0; N, 14·0%); *benzoyl derivative*, crystallising from methanol in needles, m. p. 138—139° (Found: C, 69·8; H, 7·5; N, 5·1. $C_{16}H_{21}O_3N$ requires C, 69·8; H, 7·7; N, 5·1%); *toluene*-p-*sulphonyl derivative*, crystallising from benzene–light petroleum (b. p. 60—80°) in plates, m. p. 141—142° (Found: C, 59·2; H, 6·9; N, 4·7. $C_{16}H_{23}O_4NS$ requires C, 59·1; H, 7·1; N, 4·3%).

trans-*Octahydro*-2-*oxoindole*.—(i) Methyl *trans*-2-amino*cyclo*hexylacetate (19·9 g.) was heated to 170° for 2 hr. at atmospheric pressure and then distilled under reduced pressure. The distillate of trans-*octahydro*-2-*oxoindole* (11·4 g., 70%), b. p. 167—168°/15 mm., quickly solidified. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave colourless needles, m. p. 82—83·5° (Found: C, 69·2; H, 9·5; N, 10·3. $C_8H_{13}ON$ requires C, 69·0; H, 9·4; N, 10·1%).

(ii) *trans*-2-Amino*cyclo*hexylacetic acid monohydrate (5 g.) was heated to about 250° for 15 min. at atmospheric pressure and then distilled under reduced pressure. The resulting *trans*-octahydro-2-oxoindole (2·8 g., 70%) crystallised from benzene–light petroleum in needles, m. p. 81·5—83°.

trans-*Octahydro*-1-*methylindole Methiodide*.—A solution of *trans*-octahydro-2-oxoindole (11·4 g.) in ether (150 c.c.) was added slowly to a solution of lithium aluminium hydride (5 g.) in ether (150 c.c.). When the initial reaction had subsided, the mixture was heated under reflux for 3 hr., cooled, and treated successively with moist ether and 20% sodium hydroxide solution (100 c.c.). The ethereal layer was then separated, dried (KOH), and evaporated. The residue of *trans*-octahydroindole was characterised by the preparation of the picrate, crystallising from benzene in rhombohedra, m. p. 150—152° (Found: N, 15·4. Calc. for $C_{14}H_{18}O_7N_4$: N, 15·8%), and the picrolonate, prisms (from ethanol), m. p. 236—237° (Found: N, 18·2. Calc. for $C_{18}H_{23}O_5N_5$: N, 18·0%) (King, Bovey, Mason, and Whitehead [1] record m. p. 147° and m. p. 234° for the picrate and picrolonate respectively).

The crude octahydroindole, 90% formic acid (20 c.c.), and 40% aqueous formaldehyde (11 c.c.) were heated under reflux for 7 hr. The mixture was cooled, basified, and extracted with ether. The combined ethereal extracts were dried (KOH) and treated with methyl iodide (10 c.c.). After 24 hr., the white precipitate of *trans*-octahydro-1-methylindole methiodide (18·5 g., 80% from the octahydro-2-oxoindole) recrystallised from acetone as plates, m. p. 236—237° (King *et al.*[1] record 229°) (Found: C, 42·9; H, 7·1; N, 4·9. Calc. for $C_{10}H_{20}NI$: C, 42·7; H, 7·2; N, 5·0%).

1-cyclo*Hex*-1′-*enylpyrrolidine* (cf. Heyl and Herr [9]).—Dry pyrrolidine (14·2 g.), freshly distilled *cyclo*hexanone (4·9 g.), and dry benzene (130 c.c.) were refluxed for 1 hr. in a Dean–Stark separator. Water (1·0 g.) was collected during the first 45 min. The residual solution was heated to remove benzene and then distilled, 1-cyclo*hex*-1′-*enylpyrrolidine* (4·9 g., 65%) being obtained as a pale yellow oil, b. p. 130—133°/24 mm. (Found: C, 79·9; H, 11·2; N, 9·2. $C_{10}H_{17}N$ requires C, 79·4; H, 11·3; N, 9·3%). The *picrate* crystallised from methanol in yellow needles, m. p. 145—156° (Found: C, 50·2; H, 5·4; N, 15·0. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%).

[9] Heyl and Herr, *J. Amer. Chem. Soc.*, 1953, **75**, 1918.

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Ethyl 2-Oxocyclohexylacetate (cf. Stork, Terrell, and Szmuszkovicz [3]).—The above *cyclo*hexenylpyrrolidine (3·2 g.) in dry methanol (50 c.c.) was treated with ethyl bromoacetate (4 g.). The mixture, which became warm, was left undisturbed for 1 hr. and then refluxed for 45 min. After the addition of water (10 c.c.), the mixture was heated on the steam-bath for 30 min. and then methanol was removed by distillation The residue was poured into water and the ester was isolated by ether–extraction. Ethyl 2-oxo*cyclo*hexylacetate (1·7 g., 38%) was thus obtained as a colourless oil, b. p. 139°/19 mm. (Chatterjee [10] and Ghosh [11] record 122°/5 mm. and 130°/10 mm. respectively). The semicarbazone had m. p. 199—200° (Chatterjee records 196—197°, Ghosh 196° and Kuehl, Linstead, and Orkin [12] 195—196°). The oxime had m. p. 57—58° (R. L. St. D. Whitehead [13] gives m. p. 61°). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in needles, m. p. 132° (Found: C, 53·1; H, 5·2; N, 15·6. $C_{16}H_{20}O_6N_4$ requires C, 52·7; H, 5·5; N, 15·3%).

*Hydrogenation of Ethyl 2-Hydroxyimino*cyclo*hexylacetate*.—The oxime (4 g.) in ethanolic ammonia (50 c.c.) was hydrogenated for 4 hr. over Raney nickel at 110°/20 atm. (initial). The filtered solution was heated to remove ammonia and ethanol and then refluxed with dilute hydrochloric acid (50 c.c.) for 6 hr. Evaporation of the solution under reduced pressure gave white crystals (3 g.), m. p. 160—170°. This was probably a mixture of *cis*- and *trans*-2-amino*cyclo*hexylacetic acid hydrochlorides. Four successive recrystallisations from ethanol gave *trans*-2-amino*cyclo*hexylacetic acid hydrochloride (0·2 g.), m. p. and mixed m. p. with an authentic specimen (see above), 216—217°.

Exhaustive Methylation of trans-*Octahydroindole* (cf. Part III [1]).—A solution of *trans*-octahydro-1-methylindole methiodide (16·4 g.) in water (50 c.c.) was shaken in the dark with silver oxide, freshly prepared from silver nitrate (16 g.) and sodium hydroxide (4·8 g.). The filtered solution was evaporated under reduced pressure at 45—50° to remove water, and the syrupy quaternary hydroxide which remained was then heated at 125—180°. The residue was purified through the picrate, m. p. 158—160°, and identified as the diamino-ether (2·1 g.) (see below). The distillate was treated with solid potassium hydroxide and worked up by ether-extraction, a basic oil (5·7 g.) being obtained. Distillation of the oil gave 2 fractions:

(i) trans-*NN-dimethyl-2-vinyl*cyclo*hexylamine* (4 g.), b. p. 70—72°/11 mm., n_D^{25} 1·4678 (Found: C, 78·2; H, 12·2; N, 9·2; *C*-Me, 1·4. $C_{10}H_{19}N$ requires C, 78·3; H, 12·5; N, 9·1; *C*-Me, 0%). The base gave a picrate, m. p. 117—119°, a picrolonate, m. p .162—162·5°, and a methiodide, plates (from acetone), m. p. 201° (recorded in Part III,[1] 117—118°, 163°, and 203° respectively). The base (3·5 g.), in methanol (50 c.c.), was neutralised with hydrochloric acid and hydrogenated over 10% palladium–charcoal (1 g.) at room temperature and pressure. Isolation in the usual way gave *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine (3·2 g.), b. p. 191—192°/748 mm., n_D^{19} 1·4571 (recorded in Part I, n_D^{20} 1·4573) (Found: C, 77·3; H, 13·2; N, 9·4; *C*-Me, 4·5. Calc. for $C_{10}H_{21}N$: C, 77·3; H, 13·6; N, 9·0; *C*-Me, 9·7%). The base gave the following derivatives: picrate, plates, m. p. 123—124°, from ethanol (Found: C, 50·0; H, 6·45; N, 14·9. Calc. for $C_{16}H_{24}O_7N_4$: C, 50·0; H, 6·3; N, 14·6%); picrolonate, plates (from ethanol), m. p. 172—173° (Found: C, 57·2; H, 7·1; N, 16·8. Calc. for $C_{20}H_{29}O_5N_5$: C, 57·3; H, 7·0; N, 16·7%); hydriodide, needles (from acetone), m. p. 182—183° (Found: C, 42·8; H, 7·7. Calc. for $C_{10}H_{22}NI$: C, 42·5; H, 7·8%); methiodide, plates (from acetone), m. p. 221° (decomp.) (Found: C, 44·5; H, 8·0 Calc. for $C_{11}H_{24}NI$: C, 44·4; H, 8·1%) (recorded in Part III [1] for authentic samples of picrate, picrolonate, hydriodide, and methiodide: m. p. 126°, 170°, 182°, and 231° respectively).

(ii) Di-[2-(*trans*-2′-dimethylamino*cyclo*hexyl)ethyl] ether (1 g.), b. p. 130°/11 mm. The dipicrate crystallised from ethanol in prisms, m. p. 158—160° (recorded in Part III,[1] 161°) (Found: C, 48·9; H, 5·8. Calc. for $C_{32}H_{46}O_{15}N_8$: C, 49·1; H, 5·9%). In addition to the dipicrolonate and distyphnate described in Part III, the base also gave the following derivatives: *dimethiodide*, crystallising from slightly aqueous acetone in rhombohedral plates, m. p. 210—211° (with resolidification) (Found: C, 43·0; H, 7·6. $C_{22}H_{46}ON_2I_2$ requires C, 43·4; H, 7·6%); *dimethopicrate*, crystallising from methanol in prisms, m. p. 142—144° (Found: C, 50·5; H, 6·2. $C_{34}H_{50}O_{15}N_8$ requires C, 50·4; H, 6·2%). Distillation of the dimethohydroxide from the dimethiodide (3 g.) gave, in addition to the original diamino-ether (0·12 g.), an unsaturated

[10] Chatterjee, *J. Indian Chem. Soc.*, 1935, **12**, 591.
[11] Ghosh, *ibid.*, p. 601.
[12] Kuehl, Linstead, and Orkin, *J.*, 1950, 2213.
[13] R. L. St. D. Whitehead, D. Phil. Thesis, Oxford, 1948.

ether, probably *di*-[2-(cyclo*hex*-2′-*enyl*)*ethyl*] *ether* (0·5 g.), b. p. 180—185° (bath temp.)/15 mm., n_D^{18} 1·4950 (Found: C, 82·6; H, 11·2. $C_{16}H_{26}O$ requires C, 82·0; H, 11·2%).

The diamino-ether (0·08 g.) was heated under reflux with hydriodic acid (10 c.c.) for 20 min. The solution was cooled, diluted with glacial acetic acid (5 c.c.), and treated with zinc dust (0·5 g.), added in portions during 20 min. The mixture was finally refluxed for ½ hr., cooled, and basified with sodium hydroxide solution. Extraction with ether yielded *trans*-2-ethyl-*NN*-dimethyl*cyclo*hexylamine (0·03 g.) (picrate, m. p. and mixed m. p. 123—124°; picrolonate, m. p. and mixed m. p. 171—172°).

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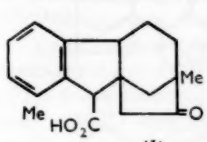
551. *Gibberellic Acid. Part IX.* The Structure of* allo*Gibberic Acid.*

By T. P. C. MULHOLLAND.

*allo*Gibberic acid, an acid-hydrolysis product of gibberellic acid, is shown to have structure (III).

*allo*GIBBERIC ACID, the unsaturated hydroxy-acid $C_{18}H_{20}O_3$ obtained by mild degradation of gibberellic acid $C_{19}H_{22}O_6$ with mineral acid,[1,2] isomerises under more vigorous conditions to the saturated keto-acid, gibberic acid, for which structure (I) has been proposed.[3,4] The present paper details and extends the evidence, described briefly in Part IV,[3] for the formulation of *allo*gibberic acid as (III).



(I)

*allo*Gibberic acid $C_{18}H_{20}O_3$ is a tetracyclic monocarboxylic acid containing an alcoholic hydroxyl group, a benzene ring, and an ethylenic bond.[1] The ultraviolet spectrum [1] (see p. 2696) shows that the aromatic ring and the ethylenic bond are not conjugated. Ozonolysis of the acid and its methyl ester yielded 0·4—0·5 mol. of formaldehyde whereas dihydro*allo*gibberic acid [1] (II) gave only a trace and was mainly recovered unchanged. The other products obtained from *allo*gibberic acid and its methyl ester were ketones containing one carbon atom less than the starting material. Thus a terminal methylene group is present in *allo*gibberic acid.

The infrared spectrum of methyl *allo*gibberate in ethylidene chloride showed a strong band near 890 cm.$^{-1}$ (=CH_2). Although methyl dihydro*allo*gibberate also absorbs in this region, the band is much weaker.

Kuhn–Roth estimations on both *allo*- and dihydro*allo*-gibberic acids gave 1·1 *C*-methyl groups; the failure to show the expected difference (cf. ref. 5) was presumably due to isomerisation of *allo*gibberic acid to gibberic acid (which also contains two *C*-methyl groups) under the strongly acid conditions used.

The alcoholic hydroxyl group present in *allo*gibberic acid is considered to be tertiary. *allo*Gibberic acid was acetylated with difficulty. Dihydro*allo*gibberic acid did not give a toluene-*p*-sulphonate or an acetate under normal conditions, although in boiling acetic anhydride a neutral gum was obtained which seemed to be mainly a mixed anhydride acetate. Similarly, attempts to oxidise the hydroxyl group to a carbonyl group in dihydro*allo*gibberic acid with chromic oxide in pyridine [6] and permanganate in acetone failed.

When dihydro*allo*gibberic acid was oxidised with alkaline permanganate the hydroxyl

* Part VIII, *J.*, 1958, 2536.

[1] Cross, *J.*, 1954, 4670.
[2] Brian, Grove, Hemming, Mulholland, and Radley, *Plant Physiol.*, 1958, in the press.
[3] Cross, Grove, MacMillan, and Mulholland, *Chem. and Ind.*, 1956, 954.
[4] *Idem, J.*, 1958, 2520.
[5] Adams and Herz, *J. Amer. Chem. Soc.*, 1949, **71**, 2546.
[6] Poos, Arth, Beyler, and Sarrett, *ibid.*, 1953, **75**, 422.

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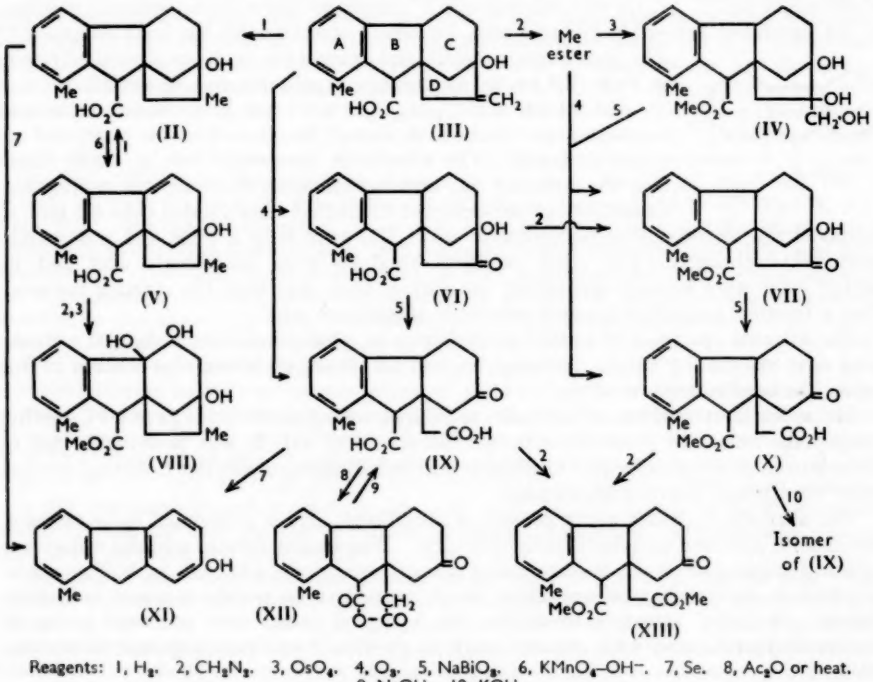
group was not attacked but a dehydro-derivative $C_{18}H_{20}O_3$ (V) was formed, in which an ethylenic bond was introduced in conjugation with the benzene ring. This reaction is analogous to the oxidation [4] of gibberic acid to dehydrogibberic acid. The dehydro-derivative (V) was converted into dihydro*allo*gibberic acid by catalytic hydrogenation and its non-crystalline methyl ester gave a crystalline diol (VIII) with osmium tetroxide.

Further evidence for the structure of *allo*gibberic acid was obtained from oxidation and dehydrogenation, summarised in the scheme. Ozonolysis of *allo*gibberic acid gave a monobasic ketol (VI), also obtained in low yield by oxidation with permanganate. The methyl ester (VII) of the ketol was obtained by ozonolysis of methyl *allo*gibberate. The second product from *allo*gibberic acid was a dibasic keto-acid (IX) whose monomethyl ester (X) was obtained by ozonolysis of methyl *allo*gibberate. Although this ester was not hydrolysed to its acid (IX) with alkali, but gave an isomer (probably owing to a stereochemical change), both the acid and the monomethyl ester (X) gave the same dimethyl ester (XIII). Oxidation of methyl *allo*gibberate with zinc permanganate or *via* the glycol (IV) followed by fission with sodium bismuthate,[7] gave the same products as ozonolysis, though in the former case a trace of a second neutral compound of unknown structure was obtained. Fission of the ketols (VI) and (VII) with sodium bismuthate yielded the corresponding keto-acids (IX) and (X).



Reagents: 1, H_2. 2, CH_2N_2. 3, OsO_4. 4, O_3. 5, $NaBiO_3$. 6, $KMnO_4$–OH^-. 7, Se. 8, Ac_2O or heat. 9, NaOH. 10, KOH.

The keto-acid (IX) formed an anhydride (XII) from which it was recovered by mild alkaline hydrolysis. Dehydration of the acid seemed to be unusually easy, the anhydride also being obtained as a product from oxidation of the ketol (VI) with bismuthate and of *allo*gibberic acid with zinc permanganate.

[7] Rigby, *J.*, 1950, 1907.

Infrared absorption maxima (cm.$^{-1}$) in solution.

Compound	Solvent	CO bands	Compound	Solvent	CO bands
(VI)	Dioxan	1751, 1734	(XIII)	$CHCl_3$	1739, 1712 (no OH)
(VII)	$CHCl_3$	1749, ~1739 (sh)			
	CCl_4	1750	(XII)	Dioxan	1813, 1766, ~1726
	Dioxan	1752, 1736	Succinic anhydride	$CHCl_3$	1871, 1791
(IX)	Dioxan	1735 (broad)	Glutaric anhydride	$CHCl_3$	1815, 1767
(X)	Dioxan	1730, 1715 (sh)			

The ketol (VI) and its ester (VII), which showed reducing properties and were split by sodium bismuthate,[7] must be α-ketols; as expected from the evidence described above they were stable to bismuth oxide in acetic acid [8] and therefore contain a tertiary hydroxyl group.

The infrared spectra in solution (see Table) of the ketols showed a high-frequency band at *ca.* 1750 cm.$^{-1}$. This band was absent from the spectrum of the 2 : 4-dinitrophenylhydrazone of the ketol (VII) and is most reasonably assigned to a carbonyl group present in a saturated five-membered ring, the frequency being raised (cf. gibberone,[4] 1745 cm.$^{-1}$ in CCl_4) by the presence of an adjacent hydroxyl group.[9]

The tertiary hydroxyl group was shown to be situated on a saturated six-membered ring by the oxidation of the ketol (VI), without loss of carbon atoms, to the dibasic keto-acid (IX). The infrared spectrum of the dimethyl ester (XIII) indicated a carbonyl group in a saturated six-membered ring, the bands in the carbonyl-stretching region being at 1712 (*cyclo*hexanone-carbonyl) and 1739 cm.$^{-1}$ (ester-carbonyl).

Dehydrogenation of the dibasic acid (IX) and of dihydro*allo*gibberic acid with selenium established the position of the tertiary hydroxyl group, and hence one point of attachment of the five-membered ring on the hexahydrofluorene skeleton of the ketols and *allo*gibberic acid. While *allo*gibberic acid, like gibberic acid,[10] gave mainly 1 : 7-dimethylfluorene (gibberene), little if any of this compound was obtained from dihydro*allo*gibberic acid. This, and more readily the keto-acid (IX), gave as the main product a fluorenol whose structure was established as 7-hydroxy-1-methylfluorene (XI) by comparison with a specimen prepared by unambiguous synthesis.[11] The fluorenol was also shown to be identical with " phenol C," obtained in low yield by selenium dehydrogenation of gibberic acid.[4] *

In the dehydrogenation of the acid (IX) to the fluorenol (XI) all the non-skeletal carbon atoms were eliminated except the aromatic *C*-methyl group. Thus the second point of attachment of the five-membered ring in the ketol and in *allo*gibberic acid is angular, as in (VI) and (III) respectively. The alternative angular position does not accommodate either a five-membered ring D or the formation of the dehydro-derivative (V) of dihydro-*allo*gibberic acid. Moreover, the infrared spectrum (Table) of the anhydride (XII) showed it to contain a six-membered anhydride ring. The carboxyl group in *allo*gibberic acid must occupy the same position as in gibberic acid (I) since methyl *allo*gibberate was converted into methyl gibberate by boiling dilute hydrochloric acid. The six-ring anhydride from (IX) can therefore only be formulated as (XII).

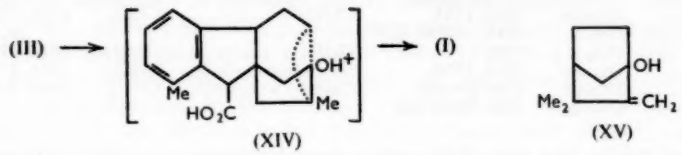
These facts establish the structure of *allo*gibberic acid as (III). The isomerisation of *allo*gibberic acid to gibberic acid can be explained by the Wagner–Meerwein mechanism,

* Since the publication of a brief report [8] of the isolation and synthesis of 7-hydroxy-1-methylfluorene, Professor Y. Sumiki of the University of Tokyo has isolated it [12] from gibberellin A_1 methyl ester (methyl α-dihydrogibberellate [13]) by ozonolysis and dehydrogenation, essentially as described above for *allo*gibberic acid.

[8] Rigby, *J.*, 1951, 793.
[9] Jones and Roberts, *Chem. and Ind.*, 1957, 1269.
[10] Mulholland and Ward, *J.*, 1954, 4676.
[11] Morrison and Mulholland, following paper.
[12] Seta, Kitamura, Takahashi, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1957, **21**, 73.
[13] Grove, Jeffs, and Mulholland, *J.*, 1958, 1236.

XUM

via the intermediate cation (XIV), in the same way that 1-hydroxycamphene (XV) gives camphor.[14]



(XIV) (XV)

Experimental

Some microanalyses are by Messrs. W. Brown and A. G. Olney. Absorption spectra (in ethanol) and alumina for chromatography were obtained as described previously.[10] Unless otherwise stated the infrared spectra were determined on Nujol mulls.

allo*Gibberic Acid.*[2]—The acid (Found: *C*-Me, 5·7; active H, 0·91. Calc. for $C_{18}H_{20}O_3$: 1 *C*-Me, 5·3; 2 active H, 0·70%) had ultraviolet max. at ~259, 264, 273, ~287, ~297 mμ (log ε 2·47, 2·51, 2·35, 1·28, 1·25 respectively).

The *methyl ester*, prepared with diazomethane, crystallised from ether–light petroleum (b. p. 40—60°) in needles, m. p. 98—99° (Found: C, 76·65; H, 7·4; OMe, 10·45. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·4; OMe, 10·4%), $\nu_{max.}$ 1734 (ester-carbonyl) and 3310 cm.$^{-1}$ (OH).

*allo*Gibberic acid was recovered after treatment with acetic anhydride and pyridine at room temperature for 24 hr. *allo*Gibberic acid (99 mg.) was kept with acetic anhydride (0·6 ml.) in pyridine (1·2 ml.) at 37° for 7 days. The gum obtained by pouring the mixture on ice and dilute hydrochloric acid and recovery in ether crystallised from ether, giving the *acetate* (54 mg.), which recrystallised as prisms, m. p. 200—204° (darkening) (Found: C, 73·7; H, 7·0; Ac, 16·9. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8; 1Ac, 13·2%), soluble in cold sodium carbonate solution, $\nu_{max.}$ 1743 (ester), 1691 (CO_2H), 1659, and 3100—3300 (OH) cm.$^{-1}$.

*allo*Gibberic acid was recovered (95%) after being heated with N-sodium hydroxide in nitrogen for 1 hr.

Oxidation.—(i) *allo*Gibberic acid (284 mg.) in sodium hydrogen carbonate (6 ml.) was treated dropwise at 0—5° with 5% aqueous potassium permanganate (12·0 ml.) in 30 min. The clear solution obtained by treatment with sulphur dioxide was acidified with hydrochloric acid and extracted with ether. Evaporation of the extract at room temperature followed by crystallisation of the residue (85 mg.) from ethyl acetate gave colourless needles of the *ketol* (VI) (29 mg.), m. p. 248—250° (decomp.) (Found: C, 71·6; H, 6·5. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). Purer specimens were obtained by ozonolysis of *allo*gibberic acid (see below).

(ii) *allo*Gibberic acid (284 mg.) in acetone (50 ml.) was treated dropwise at 20° with 6·9% aqueous zinc permanganate (5·0 ml.) in 33 min. After a further 10 min. the precipitate was filtered off, and the weakly pink colour of the filtrate did not fade during a further 30 min. Excess of permanganate was decomposed with ethanol, and the filtered solution was evaporated to dryness *in vacuo* at 25°. The residue was washed with ether–methanol [giving a gum (26 mg.)] and acetone, leaving sparingly soluble crystals (17 mg.) (A). Concentration of the acetone filtrates gave starting material (35 mg.).

Product A crystallised from ethyl methyl ketone in needles and prisms of the *anhydride* (XII), m. p. 279—281° (decomp.) (Found: C, 71·6; H, 5·9. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%). The infrared spectrum was identical with that of a specimen prepared from acid (IX) (see below).

(iii) *Ozonolysis.* (*a*) A current of ozone-enriched oxygen (3 mg. of O_3 per min.) was passed at 100 ml. per min. through a solution of *allo*gibberic acid (284 mg.) in acetic acid (10 ml.) at 22° for 26 min. (estimated ozone absorption 1·1 mol.). The mixture was diluted with water and steam-distilled. Aliquot parts of distillate were treated with an equal volume of saturated aqueous dimedone and kept at room temperature for 48 hr. Crystals of the dimedone derivative of formaldehyde (120 mg., 0·41 mole), m. p. 180—184°, separated from the first 150 ml. of distillate. Recrystallisation from 50% ethanol gave needles, m. p. 186—188°, identical (mixed m. p. and infrared spectrum) with an authentic specimen.

[14] Forster, *J.*, 1901, **79**, 644.

The yellow emulsion which formed on cooling the fraction not volatile in steam was shaken with benzene. The benzene–aqueous mother-liquors were separated from the resulting sticky solid (115 mg.) which crystallised from ethyl methyl ketone–ethyl acetate, giving (i) needles (43 mg.), m. p. 255° (decomp.), (ii) needles (29 mg.), m. p. 235—245° (decomp.), and (iii) yellowish crystals, decomp. 220—230°. Further crystallisation of fractions (i) and (ii) gave needles, m. p. 258—260° (decomp.), $[\alpha]_D^{19}$ −69° ± 3° (*c* 1·11 in EtOH) of the ketol (VI), identical (infrared spectrum) with the product obtained by oxidation with permanganate (above) [Found: C, 71·5; H, 6·6%; *M* (Rast), 298; equiv., 278, 287. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%; *M*, 286], $\lambda_{max.}$ ~249, 260, ~261, ~268, 290, 301 mμ (log ε 2·90, 3·03, 3·02, 2·98, 2·34, 2·33 respectively). Microhydrogenation did not reveal ethylenic unsaturation. The compound gave a mirror with Tollens's reagent but did not restore the colour to Schiff's reagent or give more than a weak pink colour with 1 : 4-dihydroxynaphthalene in acetic–hydrochloric acid. It did not give a black precipitate with bismuth oxide in acetic acid at 100°.

The *methyl ester* (VII), prepared with diazomethane in ether–methanol, crystallised from ether–light petroleum in prisms and needles, m. p. 130—132°, $[\alpha]_D^{19}$ −57° ± 3° (*c* 0·56 in EtOH) (Found: C, 71·8; H, 6·9; OMe, 10·4; active H, 0·38. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; 1OMe, 10·3; 1 active H, 0·33%), $\lambda_{max.}$ ~260, 265, 274, ~290, 300 mμ (log ε 2·52, 2·57, 2·45, 1·86, 1·86 respectively). The compound was neutral, absorbed no hydrogen in the presence of palladium–carbon in acetic acid, and gave a silver mirror with Tollens's reagent. It did not restore the colour to Schiff's reagent or give a black precipitate with bismuth oxide in hot acetic acid.

The orange-yellow 2 : 4-*dinitrophenylhydrazone* of the ester (VII), obtained in low yield by treatment with Brady's reagent, was absorbed on alumina, eluted with benzene containing 1% of methanol, and crystallised from benzene–ether; it had m. p. 250—254° (Found: N, 11·6. $C_{24}H_{24}O_7N_4$ requires N, 11·7%), $\nu_{max.}$ 1719 cm.$^{-1}$ (ester carbonyl).

Evaporation of the benzene–water mother-liquors from the ozonolysis gave a gum (0·19 g.) from which a small amount of an acid, m. p. 210—220° (decomp.), was isolated, identical with the acid (IX) obtained in the following experiment.

(*b*) *allo*Gibberic acid (500 mg.) was ozonised as described above, giving the crude ketol (VI) [154 mg.; m. p. 235—245° (decomp.)]. The gum recovered from the benzene–aqueous mother-liquors was kept with a little ethyl acetate until no more crystals formed; these gave the *keto-acid* (IX) [37 mg.; m. p. 210—215° (decomp.)] which crystallised from ethyl methyl ketone–ethyl acetate in prisms, m. p. 217—219° (gas evolution) followed by partial solidification and remelting at *ca.* 280° (decomp.), $[\alpha]_D^{23}$ −112° ± 3 (*c* 1·27 in EtOH) [Found: C, 67·0; H, 6·0%; equiv., 150. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; equiv. (dibasic), 151]. The acid was also obtained by further oxidation of the ketol (VI) (see below). It did not restore the colour to Schiff's reagent or react with bismuth oxide, but slowly reduced Tollens's reagent.

The *dimethyl ester* (XIII), prepared with diazomethane, crystallised from methanol in prisms, m. p. 205—207° (Found: C, 68·7; H, 6·8; OMe, 19·7. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7; 2OMe, 18·8%), insoluble in cold sodium hydroxide solution.

Preparation of the Anhydride (XII).—(i) The keto-acid (IX) was heated at 220° until gas evolution ceased and the product crystallised from ethyl methyl ketone, giving the anhydride, m. p. 279—281° (decomp.). (ii) The acid (100 mg.) was heated under reflux for 1 hr. with acetic anhydride (1·2 ml.). On cooling, the *anhydride* (61 mg.) crystallised. Further crystallisation gave needles, m. p. 285—287° (decomp.), identical (infrared spectrum) with material obtained as in (i) and by oxidation of the ketol (VI) (see below) (Found: C, 71·6; H, 5·8. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%), $\lambda_{max.}$ 267, ~271, 275 mμ (log ε 2·55, 2·48, and 2·43 respectively).

The anhydride (38 mg.) was dissolved in warm 3N-sodium hydroxide (0·78 ml.). Acidification of the cooled solution with hydrochloric acid, filtration of the resultant precipitate, and crystallisation from ethyl methyl ketone–light petroleum (b. p. 40—60°) gave prisms (26 mg.), m. p. 216—218° (decomp.), identified as the keto-acid (IX) (mixed m. p. and infrared spectrum) (Found: C, 67·9; H, 6·2. Calc. for $C_{17}H_{18}O_5$: C, 67·5; H, 6·0%).

Oxidation of Ketol (VI) *with Sodium Bismuthate.*—The ketol (250 mg.) was shaken with "AnalaR" sodium bismuthate (600 mg.) and acetic acid (8·0 ml.) at room temperature for 25 hr. After dilution with water the mixture was extracted with ether (A) and then benzene (B). The gummy crystals (0·17 g.) recovered from (A) were extracted with a little hot methanol. The residue [15 mg.; m. p. 279—281° (decomp.)] was combined with the crystals recovered

from (B) [75 mg.; m. p. 275—280° (decomp.)] and crystallised from ethyl methyl ketone, giving prisms of the anhydride (XII), m. p. 285—287° (decomp.).

Fractional crystallisation of the methanol-soluble fraction (above) from ethyl acetate and ethyl methyl ketone gave mixed fractions and the keto-acid (IX) [75 mg.; m. p. 203—215° (decomp.)] which on further crystallisation from ethyl acetate–light petroleum formed prisms, m. p. 218—220° (decomp.), identified by the infrared spectrum.

Degradation of Methyl allo*Gibberate.*—(1) *Acid hydrolysis.* (*a*) Methyl *allo*gibberate (40 mg.) in methanol (1·35 ml.) was heated under reflux in a slow stream of hydrogen chloride for 2 hr. Most of the excess of hydrogen chloride was removed in a stream of dry air, the mixture was diluted, and the neutral product (34 mg.) recovered in ether. Crystallisation from light petroleum gave hexagonal plates of methyl gibberate, m. p. and mixed m. p. 109—111°. (*b*) Methyl *allo*gibberate (124 mg.) was heated in dilute hydrochloric acid (20 ml.; 1 vol. of concentrated acid plus 5 vols. of water) under reflux for 1 hr. The neutral product (112 mg.; m. p. 102—108°), recovered in ether, crystallised in plates of methyl gibberate, m. p. and mixed m. p. 109—111°.

(2) *Oxidation.* (a) *Ozonolysis.* A current of ozonised oxygen (100 ml./min. = 3·1 mg. of O_3 per min.) was passed into a solution of methyl *allo*gibberate (200 mg.) in acetic acid (10 ml.) for 18 min. at 24°, until absorption of ozone became slow. The solution was diluted with water (10 ml.) and steam-distilled. Treatment of the distillate with saturated dimedone solution (cf. above) gave 92 mg. (0·47 mol.) of the dimedone derivative of formaldehyde.

The residue not volatile in steam was extracted with benzene. The extract was washed with sodium carbonate solution and water, dried (Na_2SO_4), and evaporated, giving a gum (101 mg.). This was chromatographed in benzene on alumina (10 × 1·0 cm.) in ultraviolet light. A light blue fluorescent band was eluted with benzene–methanol (50 : 1). The gum recovered crystallised on the addition of a little ether, giving the methyl ester (VII) (31 mg.), m. p. 123—128°, identified by mixed m. p. and infrared spectrum.

The sodium carbonate extract was acidified with hydrochloric acid and extracted with benzene. Recovery gave a gum which crystallised from ether in prisms (43 mg.), m. p. 232—235° (decomp.), raised to 239—241° (decomp.) by further crystallisation from ethyl methyl ketone–light petroleum (b. p. 60—80°), of the *keto-acid* (X), $[\alpha]_D^{21}$ −66° ± 3° (*c* 1·37 in EtOH) (Found: C, 67·8; H, 6·5; OMe, 9·7; active H, 0·41%; equiv., 304, 321. $C_{18}H_{20}O_5$ requires C, 68·3; H, 6·4; 1OMe, 9·8; 1 active H, 0·32%; *M*, 316), $\lambda_{max.}$ ~261, 266, 274 mμ (log ε 2·44, 2·63, 2·34 respectively). The acid was sparingly soluble in cold ethyl acetate; in later experiments gums were removed by washing the crude crystals with ethyl acetate. It dissolved in sodium hydroxide but only slowly in sodium carbonate solution. It did not restore the colour to Schiff's reagent, give a red colour with naphthalene-1 : 4-diol in acetic–hydrochloric acid, or reduce bismuth oxide in acetic acid. It gave a precipitate with Brady's reagent.

The *oxime*, prepared in pyridine, crystallised from ethanol or methanol in needles, m. p. 244° (decomp.) (Found: N, 4·5. $C_{18}H_{21}O_4N$ requires N, 4·4%).

The dimethyl ester (XIII) crystallised from methanol in prisms, m. p. 205—207° (darken), identical (mixed m. p. and infrared spectrum) with material obtained by methylation of acid (IX) (see above).

The keto-acid (X) (50 mg.) was kept in 20% potassium hydroxide solution (2·0 ml.) at room temperature for 4 days. Acidification with hydrochloric acid followed by ether-extraction and recovery from the extract gave a gum (54 mg.). An ethereal solution of the gum deposited crystals; more crystalline material was obtained by gradual addition of light petroleum (b. p. 40—60°). The crystalline product (37 mg.) recrystallised from ethyl methyl ketone–light petroleum (b. p. 60—80°) in prisms, m. p. 247—249° (decomp.), of a *dibasic acid*, $[\alpha]_D^{19}$ −67° ± 3° (*c* 0·54 in EtOH) [Found: C, 67·6; H, 6·1%; equiv., 168. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; equiv. (dibasic), 151]. The acid was different (infrared spectrum) from the isomer (IX) obtained by oxidation of *allo*gibberic acid and by hydrolysis of the anhydride (XII).

(b) *With osmium tetroxide.* A mixture of methyl *allo*gibberate (92 mg.), pyridine (75 mg.), and osmium tetroxide (105 mg.) in benzene (12 ml.) was kept in the dark at room temperature for 13 days, then evaporated to dryness *in vacuo*. The residue was shaken in methylene chloride (25 ml.) with a 10% solution of mannitol in 1% potassium hydroxide (20 ml.) for 15 min. The organic layer was washed with the mannitol solution and with water, dried (Na_2SO_4), and evaporated, giving a solid (70 mg.), m. p. 186—192°, which crystallised from benzene–light petroleum (b. p. 60—80°) in long needles of the *glycol* (IV) (59 mg.), m. p. 190—194°, raised to

192—194·5° by recrystallisation (Found: C, 68·3; H, 7·3; active H, 0·88. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3; 1 active H, 0·90%), $\nu_{max.}$ 3380 and 3500 (OH), 1717 cm.$^{-1}$ (ester).

(c) *Fission of the glycol* (IV). (i) The glycol (100 mg.) in benzene (20 ml.) at 40° was treated with lead tetra-acetate (230 mg.) in benzene (10 ml.). After being heated under reflux for 5 min. and kept for 1 hr. at room temperature (no excess of reagent present) the mixture was filtered. The filtrate was extracted with sodium carbonate solution, washed with water, dried, and evaporated, giving a gum (74 mg.). The alkaline extract was acidified and extracted with benzene and with ether. The water-washed and dried extracts were evaporated, giving a semi-crystalline residue (14 mg.) which crystallised from aqueous ethanol in prisms, m. p. 239—241° (decomp.), of the keto-acid (X). The yield of crystalline material was not increased when more reagent was used.

(ii) A mixture of the glycol (700 mg.) and " AnalaR " sodium bismuthate (1·250 g.) in acetic acid (7·0 ml.) was shaken at room temperature until the solution was almost clear and colourless (5·5 hr.). The mixture was diluted with water and extracted with benzene. The benzene was washed with water, extracted with sodium carbonate solution, washed, dried, concentrated to 5 ml., and chromatographed on alumina (20 × 1·3 cm.). Elution with benzene–methanol in ultraviolet light gave fractions (*x*) (50 : 1) a blue fluorescent band, giving a gum (329 mg.) on recovery, and (*y*) (20 : 1) a diffuse blue band, giving a gum (112 mg.) on recovery. A benzene solution of material from fraction (*x*) was gradually diluted with light petroleum (b. p. 40—60°) at 0°, giving a solid (232 mg.), m. p. 117—123°. Recrystallisation gave needles of the ketol ester (VII), m. p. 129—131°, identified by mixed m. p. and infrared spectrum. The sodium carbonate extract was acidified and the product recovered in benzene as a mixture of gum and crystals (61 mg.) which crystallised from ethyl methyl ketone–light petroleum (b. p. 60—80°) in prisms of the keto-acid (X), m. p. 239—241° (decomp.), identified by analysis, mixed m. p., and infrared spectrum.

(d) *With zinc permanganate.* 6·7% Aqueous zinc permanganate (22·0 ml.) was added in one lot to methyl *allo*gibberate (1·14 g.) in acetone (200 ml.) at 21°. When the reagent was consumed (90 min.) the mixture was filtered. The combined filtrate and acetone washings of the precipitate were concentrated *in vacuo* below 30°. The residue was extracted with benzene and ether. The combined extracts were extracted 3 times with sodium hydrogen carbonate solution, then repeatedly with 2% aqueous sodium hydroxide until the aqueous layer was nearly colourless. The neutral fraction was recovered and treated with ether, giving sticky crystals (0·10 g.) (A) and a gummy residue (0·41 g.) (B). Material (B) was chromatographed in ether on alumina (20 × 2·2 cm.) and eluted in 75 ml. fractions, from which gums were recovered, as follows: 1—5 (ether), 97 mg.; 6—8 [ether–methanol (100 : 1)], 106 mg.; 9—12 [ether–methanol (50 : 1)], 57 mg. On treatment with ether, fractions 9—12 gave crystals (7 mg.) which crystallised from ether–light petroleum in needles, m. p. 126—130°, identified (mixed m. p. and infrared spectrum) as the ketol-ester (VII). Material (A) was crystallised several times from ether–methanol and from ether methyl ketone–light petroleum (b. p. 60—80°), giving a *substance* of unknown structure as needles, m. p. 195—197° (16 mg.) (Found: C, 72·0; H, 7·0; OMe, 10·1; active H, 0·33. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7; 1OMe, 10·3; 1 active H, 0·33%), $\nu_{max.}$ 1720 (C=O), 3400 cm.$^{-1}$ (alcoholic OH).

The sodium hydrogen carbonate extract was acidified with hydrochloric acid and extracted with ether and benzene. Recovery gave a gum (186 mg.) which crystallised from ether as prisms, identified (infrared spectrum) as the keto-acid (X) (139 mg.; m. p. 225—230°) which had m. p. 233—236° (decomp.) (104 mg.) on crystallisation from ether–ethyl methyl ketone.

Oxidation of the Ketol-ester (VII).—(1) *With zinc permanganate.* The compound (150 mg.) in acetone (20 ml.) was treated with 6·7% zinc permanganate solution (1·1 ml.) and kept at room temperature until the reagent was consumed (3·5 hr.). The mixture was filtered and the filtrate and acetone washings were evaporated *in vacuo*. An ethereal solution of the residual gum was extracted with sodium carbonate solution. Recovery of the neutral fraction gave starting material (41 mg.), m. p. 130—132°, identified by the infrared spectrum. The neutral compound, m. p. 195—197° (obtained by the oxidation of methyl *allo*gibberate with zinc permanganate), was not obtained. Recovery from the sodium carbonate extract gave the keto-acid (X) (12 mg.) which crystallised from acetone–ether in prisms, m. p. 235—239° (decomp.).

(2) *With sodium bismuthate.* The compound (25 mg.) was shaken with " AnalaR " sodium bismuthate (50 mg.) in acetic acid (0·6 ml.) at room temperature for 3 hr. The mixture was diluted with water and extracted with benzene. The benzene extract was extracted with

sodium carbonate solution. Recovery of the neutral fraction gave a gum (4 g.). Recovery of the acid fraction gave the keto-acid (9 mg.), which crystallised from acetone–ether in prisms (8 mg.), m. p. 235—238° (decomp.), identified by infrared spectrum and mixed m. p.

*Dihydro*allo*gibberic Acid.*—The following preparation gave a product of higher m. p. than that previously described.[1] *allo*Gibberic acid (3·00 g.) in methanol (120 ml.) was hydrogenated at room temperature and pressure in the presence of Adams catalyst (200 mg.). Uptake of hydrogen ceased after the absorption of 1·05 mol. in 30 min., and crystals of the product separated. The mixture was filtered. Evaporation of the combined filtrate and acetone washings gave a solid which was dried by distillation with toluene and crystallised from toluene–methanol as prisms (2·61 g.) of dihydro*allo*gibberic acid, m. p. 200—203°. Further crystallisation raised the m. p. to 204—207°. This product had $[\alpha]_D^{21}$ −67° ± 3° (*c* 0·96 in EtOH) (Found: C, 75·4; H, 7·8; *C*-Me, 5·6; active H, 0·79. Calc. for $C_{19}H_{22}O_3$: C, 75·5; H, 7·7; 2 *C*-Me, 10·5; 2 active H, 0·70%). Concentration of the mother-liquors gave a further crop (0·38 g., m. p. 199—202°). Dihydro*allo*gibberic acid crystallised from water in needles of the *hydrate*, m. p. 204—207° (shrinking at *ca.* 130—144°) (Found, after drying at 20°: C, 71·2; H, 8·0. $C_{19}H_{22}O_3,H_2O$ requires C, 71·0; H, 7·95%). Like *allo*gibberic acid,[2] anhydrous dihydro-*allo*gibberic acid showed a double peak in the carbonyl stretching region at 1715 and 1687 cm.$^{-1}$, whereas the hydrate showed a sharp band at 1700 cm.$^{-1}$. Ultraviolet max. were at ~260, 264, 273 mμ (log ε 2·18, 2·24, 2·08 respectively). The methyl ester did not crystallise.

Dihydro*allo*gibberic acid was recovered (86%) after 1 hour's heating with N-hydrochloric acid.

*Acylation of Dihydro*allo*gibberic Acid.*—(*a*) The compound was stable to acetic anhydride in pyridine during 40 hr. at room temperature.

(*b*) The compound (104 mg.) was kept at 35° wth acetic anhydride (0·60 ml.) in pyridine (1·20 ml.) for 7 days Treatment with ice and hydrochloric acid and recovery of the *acetate* in ether gave a glass (101 mg.) (Found: C, 73·05; H, 7·6; Ac, 17·4. $C_{20}H_{24}O_4$ requires C, 73·1 H, 7·4; 1Ac, 13·1%). The glass dissolved readily in cold sodium carbonate solution. The infrared spectrum showed hydroxyl bands (3100—3400 cm.$^{-1}$), strong bands at 1738 and 1706 cm.$^{-1}$, and very weak absorption at *ca.* 1800—1810 cm.$^{-1}$.

(*c*) The compound (150 mg.) was heated under reflux with acetic anhydride (10 ml.) for 6 hr. The product obtained by evaporation was passed through a column of alumina in ether and recovered as a glass (136 mg.) (Found: Ac, 21·4. Calc. for $C_{22}H_{26}O_5$: 2Ac, 23·2%). The glass did not dissolve readily in cold sodium carbonate solution. An infrared spectrum showed C=O absorption at 1813 and 1737 cm.$^{-1}$ and no hydroxyl absorption. Treatment of the glass with boiling water or cold 1% sodium hydroxide solution gave an acidic glass whose infrared spectrum approximated to the above acetate but a very weak band at *ca.* 1810 cm.$^{-1}$ persisted.

(*d*) Treatment of the compound with toluene-*p*-sulphonyl chloride in pyridine for 68 hr. at room temperature gave starting material.

*Oxidation of Dihydro*allo*gibberic Acid.*—(*a*) The compound (100 mg.) in pyridine (1·0 ml.) was added to chromium trioxide (100 mg.) in pyridine (1·0 ml.). The mixture was kept at room temperature for 18 hr. Only starting material (74 mg.) was recovered.

A solution of the compound (28·6 mg.) in acetone (1 ml.) was treated with potassium permanganate (11 mg.) in water (0·50 ml.). After 18 hr. at room temperature, recovery gave starting material (11 mg.).

(*b*) The compound (572 mg.), dissolved in sodium hydrogen carbonate solution (12 ml.), was treated dropwise at 0—3° with 5% aqueous potassium permanganate (12·5 ml.) during 19 min. After 5 min. sulphur dioxide was passed into the mixture, and the solution was acidified with hydrochloric acid. The precipitate (254 mg.) was filtered off. Crystallisation from dilute methanol gave prisms (198 mg.) of the *dehydro-derivative* (V), which softened at *ca.* 115—125° (loss of solvent), giving a gum which partly resolidified and remelted at 170—172° (Found, after drying at room temperature over P_2O_5: C, 72·1; H, 7·5%; equiv., 321. $C_{18}H_{20}O_3,CH_3{\cdot}OH$ requires C, 72·1; H, 7·65%; *M*, 316). Infrared bands included broad carboxylic OH absorption, alcohol OH (3360 cm.$^{-1}$), and a C=O band (1703 cm.$^{-1}$). Ultraviolet max. were at ~250, 259, 268, 290, 300 mμ (log ε 3·98, 4·13, 4·07, 3·50, 3·46 respectively).

Crystallisation from water gave needles of a *hydrate*, softening at *ca.* 110°, becoming gummy at 118—120°, and liquid at *ca.* 150° (Found, after drying over P_2O_5 at room temperature: C, 72·9; H, 7·3. $C_{18}H_{20}O_3,\frac{2}{3}H_2O$ requires C, 73·0; H, 7·3%). The acid was soluble in cold

sodium carbonate solution and was unsaturated to permanganate in acetone. With concentrated sulphuric acid it gave a yellow colour changing to reddish purple and finally to pink.

The methyl ester, prepared with diazomethane in ether, was a gum. This (146 mg.) was kept with osmium tetroxide (142 mg.) and pyridine (154 mg.) in benzene (8 ml.) in the dark at room temperature for 13 days. After evaporation *in vacuo* a solution of the residue in methylene chloride (30 ml.) was shaken with a 10% solution of mannitol in 1% potassium hydroxide (25 ml.). The organic layer was washed with water, dried, and evaporated, giving a gum which crystallised on trituration with ether as prisms (78 mg.) of the *glycol* (VIII), m. p. 162—165°. Further crystallisation from benzene–light petroleum (b. p. 60—80°) gave needles, m. p. 169—171° (Found: C, 68·65; H, 7·3. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3%), $\nu_{max.}$ 1708 (C=O), 3320, 3400, and 3520 cm.$^{-1}$ (alcoholic OH).

Reduction of the Dehydro-derivative (V).—The compound (29 mg.) in methanol (6 ml.) was hydrogenated in the presence of Adams platinum catalyst (33 mg.) at room temperature and pressure. 1 mol. of hydrogen was absorbed and the product (29 mg.; m. p. 192—194°) crystallised from toluene in prisms, m. p. 200—202°, of dihydro*allo*gibberic acid (mixed m. p. and infrared spectrum).

Dehydrogenation.—(1) allo*Gibberic acid.* A mixture of *allo*gibberic acid (100 mg.) and selenium (100 mg.) was heated in a stream of nitrogen for 2 hr. at 360°. The product (38 mg.) collected by distillation at 15—20 mm. was chromatographed in light petroleum (b. p. 40—60°; 4 ml.) on alumina (10 × 1·0 cm.) and eluted in ultraviolet light. It afforded 1 : 7-dimethylfluorene (26 mg.), m. p. 102—105°, as sole identified product.

(2) *The keto-acid* (IX). The acid (50 mg.) and selenium (50 mg.) were heated in a stream of nitrogen at 350—360° for 200 min., then distilled at 20 mm. The distillate (18 mg.) in ether–light petroleum (b. p. 40—60°; 1 : 3) was chromatographed on alumina (10 × 0·8 cm.) in ultraviolet light, giving four fractions. Only a fraction (6 mg.) eluted with ether was tractable. It crystallised from light petroleum (b. p. 60—80°) in needles (3·5 mg.), m. p. 166—168°, of 7-*hydroxy*-1-*methylfluorene*, identical (mixed m. p. infrared and ultraviolet spectra) with an authentic specimen of the same m. p. prepared by synthesis [11] and with " phenol C " obtained by dehydrogenation of gibberic acid [4] (Found: C, 85·0, 85·7; H, 6·2, 6·8. $C_{14}H_{12}O$ requires C, 85·7; H, 6·2%). More was obtained by dehydrogenation of the gums recovered from the crystallisation mother-liquors of the keto-acid (IX) and the ketols (VI) and (VII).

The *benzoate* crystallised from dilute acetic acid or light petroleum (b. p. 80—100°) in plates, m. p. 160—161° (Found: C, 84·0; H, 5·4. $C_{21}H_{16}O_3$ requires C, 84·0; H, 5·4%), and the *acetate* from methanol in plates, m. p. 130—131° (Found: C, 80·0; H, 5·9. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%), respectively identical (mixed m. p. and infrared spectra) with authentic specimens of m. p. 159—160·5° and 131—132°.

(3) *Dihydro*allo*gibberic acid.* The compound (430 mg.) was heated with selenium for 2 hr. at 360° in a stream of nitrogen, and then distilled as described above. The distillate (180 mg.) was chromatographed in ether on alumina (24 × 1·5 cm.). Two fractions gave defined products. Fraction (ii), eluted with light petroleum containing 5—10% of ether, crystallised from methanol but the m. p. was not raised above 75—90°. Fraction (iv) (27 mg.), obtained with 20 : 3 light petroleum–ether, crystallised from dilute ethanol in small needles, m. p. 159—161°, not depressed on admixture with 7-hydroxy-1-methylfluorene. Fractions (v)—(vii) (122 mg.), eluted with light petroleum containing 20—50% of ether and with ether–methanol (20 : 1), were rechromatographed giving more (51 mg.) of the fluorenol; sublimation at 100—120°/10^{-2} mm. and several crystallisations from light petroleum gave needles, m. p. and mixed m. p. 165—168°.

The author is indebted to Dr. L. A. Duncanson for the infrared spectra, to Mr. A. Morrison for technical assitance, and to several colleagues for helpful discussion.

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552. *Gibberellic Acid. Part X.*[1] 7-*Hydroxy*-1-*methylfluorene.*

By A. Morrison and T. P. C. Mulholland.

7-Hydroxy-1-methylfluorenone and 7-hydroxy-1-methylfluorene have been synthesised. The latter is identical with the fluorenol obtained by degradation of *allo*gibberic acid.

The fluorenol obtained [1] by dehydrogenation of dihydro- and other degradation products of *allo*gibberic acid has been shown to be 7-hydroxy-1-methylfluorene by comparison with a specimen prepared as follows.

The starting material, 5-methoxy-2-nitrotoluene, is most easily prepared by nitrating *m*-methoxytoluene.[2] The scale of the reaction could be increased safely without much fall in yield although the product was contaminated with a small amount of the 4-nitro-isomer and with 3-hydroxy-2 : 4 : 6-trinitrotoluene. The 5-methoxy-2-nitrotoluene fraction was oxidised [3] with aqueous potassium permanganate to 5-methoxy-2-nitrobenzoic acid which was separated from the 4-nitro-isomer by crystallisation. 5-Methoxy-2-nitrotoluene was less readily oxidised than the 4-nitro-isomer, and when the oxidation of the mixed isomers was carried out in the presence of magnesium sulphate [4] the only acidic product was 3-methoxy-4-nitrobenzoic acid.

5-Methoxy-2-nitrobenzoic acid was more conveniently reduced to the amine by catalytic hydrogenation than by the chemical methods described in the literature. Subsequent reaction of the amine with acetic anhydride gave 6-methoxy-2-methyl-4-oxo-3 : 1-benzoxazine. This with *o*-tolylmagnesium bromide gave 2-acetamido-5-methoxy-2′-methylbenzophenone.[5] Hydrolysis of the acetyl derivative gave the amine, from which 7-methoxy-1-methylfluorenone was obtained by diazotisation and ring closure. Demethylation of the fluorenone gave 7-hydroxy-1-methylfluorenone, and reductive demethylation gave 7-hydroxy-1-methylfluorene. The latter, its acetate, and benzoate were found, by mixed melting point and infrared absorption, to be identical with the fluorenol and corresponding derivatives obtained by degradation of dihydro*allo*gibberic acid.[1] The synthetic fluorenol was also identical with " phenol C " obtained by dehydrogenation of gibberic acid.[6]

Experimental

M. p.s are corrected. The ultraviolet absorption spectrum and alumina for chromatography were obtained as described previously.[7] Microanalyses are by Messrs. W. Brown and A. G. Olney.

5-Methoxy-2-nitrotoluene.—Nitration [2] of *m*-methoxytoluene was carried out in batches on a maximum scale of 110 g. in 10-l. conical flasks. An ethereal solution of the combined crude product (from 780 g. of starting material) was shaken with aqueous sodium hydrogen carbonate. A yellow sodium salt separated (see below). The ethereal solution was washed with water, dried, and evaporated. Distillation of the residue gave 5-methoxy-2-nitrotoluene (640 g., 58%), b. p. 116—120°/4 mm., m. p. 45—47°. This material, containing some of the 4-nitro-isomer, was used for oxidation without further purification.

Addition of hydrochloric acid to an aqueous solution of the yellow sodium salt (*ca.* 40 g.) gave a precipitate of 3-hydroxy-2 : 4 : 6-trinitrotoluene, which was purified by crystallisation from benzene–light petroleum and from water (charcoal), giving pale yellow needles (31 g.), m. p. 106·5—109° (Found: C, 34·8; H, 2·0; N, 17·4. Calc. for $C_7H_5O_7N_3$: C, 34·6; H, 2·1; N, 17·3%). The recorded m. p. is 109—110°.

[1] Part IX, Mulholland, preceding paper.
[2] Cook, Dickson, Ellis, and Loudon, *J.*, 1949, 1074.
[3] Schiemann, *Ber.*, 1929, **62**, 1794.
[4] Dewar, *J.*, 1944, 619.
[5] Cf. Lothrop and Goodwin, *J. Amer. Chem. Soc.*, 1943, **65**, 363.
[6] Cross, Grove, MacMillan, and Mulholland, *J.*, 1958, 2520.
[7] Mulholland and Ward, *J.*, 1954, 4676.

5-Methoxy-2-nitrobenzoic Acid.—Oxidation of 5-methoxy-2-nitrotoluene with aqueous potassium permanganate as described by Schiemann [3] gave a 15—20% yield of crude acidic product, m. p. 122—129°. Recovered starting material was recycled until 298 g. of crude acidic product were obtained. The benzene-soluble portion was fractionally crystallised from benzene and benzene containing a little methanol (seeding), giving 5-methoxy-2-nitrobenzoic acid as large prisms and needles (220 g.; m. p. 135—136°; 21 g. of fractions of m. p. 131—136°) and fractions of small needles of 3-methoxy-4-nitrobenzoic acid, m. p. 220—230° (15 g.). The 2-nitro-isomer crystallised from benzene in pale yellow prisms, m. p. 135—136°, which became colourless and opaque on drying at 100—110° (Found: C, 48·8; H, 3·6. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·6%). Schiemann [3] records m. p. 133°, in agreement with other authors except Hodgson and Beard [8] who give m. p. 255°.

The *methyl ester* formed very pale yellow needles [from light petroleum (b. p. 40—60°)], m. p. 55—57° (Found: C, 51·1; H, 4·3; N, 6·4. $C_9H_9O_5N$ requires C, 51·2; H, 4·3; N, 6·6%).

3-Methoxy-4-nitrobenzoic acid crystallised from ethanol in colourless needles, m. p. 231—233° (Found: C, 48·7; H, 3·6%).

Attempts to improve the yield of acidic products by the use of a higher ratio permanganate : substrate and by gradual addition of the reagent failed. Oxidation in the presence of magnesium sulphate at 75—80° [4] was incomplete and gave 3-methoxy-4-nitrobenzoic acid as the only acidic product. At 100° all the reagent was consumed but the yield of acidic product did not exceed 21%. Oxidation with potassium permanganate in pyridine [7] gave a slightly better yield (26%) but was more tedious on a large scale.

2-Amino-5-methoxybenzoic Acid.—2-Methoxy-5-nitrobenzoic acid (7·6 g.) in ethanol (400 ml.) was hydrogenated at room temperature and pressure in the presence of 5% palladium–charcoal [9] (845 mg.). 3 Mol. of hydrogen were absorbed in 45 min. Evaporation of the filtered solution *in vacuo* at low temperature gave 2-amino-5-methoxybenzoic acid as a pale yellow solid, m. p. 145—147° (6·5 g.). A specimen purified by sublimation *in vacuo* followed by crystallisation from benzene–light petroleum (b. p. 40—60°) and from dilute methanol formed almost colourless needles, m. p. 148—150·5° (Found: C, 57·5; H, 5·3; N, 8·6. Calc. for $C_8H_9O_3N$: C, 57·5; H, 5·4; N, 8·4%). The m. p. has been recorded as 149—150° [10, 11] and 179—180°.[12]

2-Methyl-6-methoxy-4-oxo-3 : 1-benzoxazine.—The above crude amine (99 g.) was added in portions to acetic anhydride (540 ml.) at 130—140°. The mixture was concentrated to *ca.* 90 ml. and cooled, giving the benzoxazine (95 g.; m. p. 116—120°). Recrystallisation from acetic anhydride gave colourless needles, m. p. 119—120° (Found: C, 62·8; H, 4·9; N, 7·3. Calc. for $C_{10}H_9O_3N$: C, 62·8; H, 4·75; N, 7·3%) (lit.,[13] m. p. 124°). Hydrolysis of the benzoxazine with water at 100° gave 2-acetamido-5-methoxybenzoic acid which crystallised from water in needles, m. p. 165—166° (Found: C, 57·5; H, 5·25; N, 6·7. Calc. for $C_{10}H_{11}O_4N$: C, 57·4; H, 5·3; N, 6·7%) (lit.,[12] m. p. 161—162°).

The above acetate and diazomethane gave the *methyl ester*, which crystallised from light petroleum (b. p. 80—100°) in needles and prisms, m. p. 96—97° (Found: C, 59·5; H, 5·9; N, 6·4. $C_{11}H_{13}O_4N$ requires C, 59·2; H, 5·9; N, 6·3%).

2-Acetamido-5-methoxy-2'-methylbenzophenone.—A Grignard reagent prepared from *o*-bromotoluene (10·6 g.) and magnesium (1·6 g.) in ether (40 ml.) was filtered and added dropwise in 60 min. to a well-stirred, ice-cold solution of the benzoxazine (11·7 g.) in benzene (250 ml.). A solid separated. The mixture was heated at 30° for 1 hr., cooled, and decomposed with ice (300 g.) and 3N-sulphuric acid (180 ml.). The organic layer and ether-washing of the aqueous layer were combined, washed with water, sodium hydrogen carbonate and with water, and evaporated. The residue was steam-distilled A solution of the non-volatile fraction in ether was washed with water, dried, and evaporated, giving a solid (14·5 g.), m. p. 85—95°. In the best preparations this was pale yellow but sometimes was orange. The product in ether (700 ml.) was chromatographed on alumina (26 × 4·0 cm.). Elution with ether in ultraviolet light removed a blue fluorescent band and then a band appearing brown. Recovery of the

[8] Hodgson and Beard, *J.*, 1926, 147.
[9] Vogel, " Practical Organic Chemistry," Longmans Green & Co., London, 1948, p. 990.
[10] Pschorr, *Annalen*, 1912, **391**, 23.
[11] Smith, Elisberg, and Sherrill, *J. Amer. Chem. Soc.*, 1946, **68**, 1301.
[12] Friedlaender, *Ber.*, 1916, **49**, 955.
[13] Heilbron, Kitchen, Parkes, and Sutton, *J.*, 1925, **127**, 2167.

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latter gave a pale yellow solid (10 g.) which crystallised from light petroleum (b. p. 80—100°) and from methanol as colourless prisms (7·5 g.), m. p. 121—122°, of *2-acetamido-5-methoxy-2'-methylbenzophenone*. Further crystallisation raised the m. p. to 123—124° (Found: C, 71·7; H, 6·1; N, 4·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·05; N, 4·9%).

In later preparations the combined crude acetate (155 g.) was crystallised twice from methanol, giving 64 g., m. p. 118·5—121°. 23 g. were recovered from the mother-liquors.

2-Amino-5-methoxy-2'-methylbenzophenone.—The above amide (1·00 g.) was heated under reflux with ethanol (10 ml.) and concentrated hydrochloric acid (3 ml.) for 3·5 hr. The solution was made alkaline with dilute ammonia solution and kept at 0°, giving crystals (885 mg.) of the *amine*, m. p. 52—54·5°. Recrystallisation from dilute methanol gave prisms, m. p. 62—63° (Found: C, 74·4; H, 6·3; N, 5·9; OMe, 12·9. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3; N, 5·8; OMe, 12·9%). It regenerated the acetyl derivative, m. p. and mixed m. p. 120°.

7-Methoxy-1-methylfluorenone.—A solution of the above crude amine (2·0 g.) in 25% hydrochloric acid (250 ml.) was diazotised at 0—5° with sodium nitrite (0·70 g.) in water (5 ml.). The solution was allowed to warm to room temperature, then heated at 100° for 2 hr. and under reflux for 2·5 hr. An ethereal extract of the cooled mixture was washed with dilute sodium hydroxide and with water, treated with charcoal, dried, and evaporated. A solution of the residue (1·15 g.) in ether–light petroleum (b. p. 40—60°, 6 : 1) was chromatographed on alumina (1·5 × 12 cm.). Elution with the same solvent in ultraviolet light removed a brown band from which a solid was recovered (642 mg.; m. p. 80·5—83°). Crystallisation from methanol gave the *fluorenone* as orange-yellow needles (538 mg.), m. p. 83—84° raised to 84—84·5° by recrystallisation (Found: C, 80·45; H, 5·5; OMe, 14·1. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·4; OMe, 13·8%). The *oxime*, prepared in pyridine, crystallised from light petroleum (b. p. 80—100°) in pale greenish-yellow needles, m. p. 185—186° (Found: C, 74·9; H, 5·3; N, 5·8. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·5; N, 5·85%). The *2 : 4-dinitrophenylhydrazone* crystallised from nitrobenzene–acetic acid in red needles, m. p. 275·5—276·5° (Found: C, 62·7; H, 4·2; N, 14·3. $C_{21}H_{16}O_5N_4$ requires C, 62·4; H, 4·0; N, 13·9%).

7-Hydroxy-1-methylfluorene.—7-Methoxy-1-methylfluorenone (908 mg.) was heated with acetic acid (7·5 ml.), red phosphorus (100 mg.), and hydriodic acid (6 ml.; *d* 1·66) for 96 hr. A filtered ethereal extract of the crude mixture was washed with water, sodium carbonate solution, dilute sodium dithionite solution, and water, dried, and evaporated, giving a solid (868 mg.). This was chromatographed in 1 : 1 ether–light petroleum (b. p. 40—60°) on alumina (1·6 × 22 cm.). Elution with the same solvent removed a light blue fluorescent band, from which an almost colourless solid (509 mg.; m. p. 150—165°) was recovered. Sublimation *in vacuo* followed by crystallisation from benzene–light petroleum (b. p. 80—100°) gave needles of 7-hydroxy-1-methylfluorene (402 mg.), m. p. 161—165°, raised to 166—168° by recrystallisation (Found: C, 85·45, 86·1; H, 6·5, 6·0. Calc. for $C_{14}H_{12}O$: C, 85·7; H, 6·2%), $\lambda_{max.}$ (in EtOH) 274, ~283, 304, ~313 mμ (log ε 4·26, 4·17, 3·70, 3·66 respectively). The acetate crystallised from methanol in plates, m. p. 131—132° (Found: C, 80·5; H, 5·8. $C_{16}H_{14}O_2$ requires C, 80·6; H, 5·9%). The benzoate (cf. ref. 14) crystallised from dilute acetic acid or light petroleum (b. p. 80—100°) in plates, m. p. 159—160·5° (Found: C, 83·8; H, 5·5. Calc. for $C_{21}H_{16}O_2$: C, 84·0; H, 5·4%).

The *methyl ether* crystallised from ethanol in colourless plates, m. p. 111—112·5° (Found: C, 85·7; H, 6·9; OMe, 14·6. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7; 1OMe, 14·8%). The *1 : 3 : 5-trinitrobenzene adduct* of the methyl ether crystallised from ethanol in red needles, m. p. 97—98° (Found: C, 59·2; H, 4·3; N, 10·3. $C_{15}H_{14}O,C_6H_3O_6N_3$ requires C, 59·6; H, 4·05; N, 9·9%). The *adduct* of the methyl ether with 3-hydroxy-2 : 4 : 6-trinitrotoluene crystallised from ethanol in bronze needles, m. p. 128·5—130° (Found: C, 58·1; H, 4·4; N, 9·7. $C_{15}H_{14}O,C_7H_5O_7N_3$ requires C, 58·3; H, 4·2; N, 9·3%).

7-Hydroxy-1-methylfluorenone.—7-Methoxy-1-methylfluorenone (1·00 g.) was heated with 48% hydrobromic acid (40 ml.) and acetic acid (10 ml.) for 3·5 hr., then cooled. The red precipitate was washed with water, dried, and chromatographed in ether on alumina (20 × 3·0 cm.). Elution with ether removed a yellow band from which starting material was recovered, and further elution with ether–methanol (99 : 1) removed a red band. Recovery of the latter gave a solid (720 mg.) which crystallised from ethanol in red needles (640 mg.) of the *hydroxyfluorenone*, m. p. 178·5—180°, raised to 183—184° by recrystallisation (Found: C, 79·7; H, 4·65. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%). The *acetate* crystallised from methanol in

[14] Kliegl, Wunsch, and Weigele, *Ber.*, 1926, **59**, 631.

yellow needles, m. p. 138—140° (Found: C, 76·4; H, 4·9. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%). The *oxime* of the hydroxyfluorenone crystallised from toluene in yellow-green needles, m. p. 228·5—230° (Found: C, 74·8; H, 5·15; N, 6·7. $C_{14}H_{11}O_2N$ requires C, 74·65; H, 4·9; N, 6·2%).

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553. *The Catalytic Hydrogenation of Unsaturated Hydrocarbons. Part I. The Kinetics of the Hydrogenation of Acetylene over a Nickel–Pumice Catalyst.*

By G. C. BOND.

The kinetics of acetylene hydrogenation over a nickel–pumice catalyst have been studied in a static system under a wide variety of conditions between 80° and 110° c. The kinetic form of pressure–time curves depends on (i) the initial hydrogen : acetylene ratio, (ii) the order of addition of the reactants if added separately, and (iii) the pretreatment of the catalyst, if the reactants are added together. When acetylene is added first, the pressure–time curves are of the first order in hydrogen if the initial hydrogen : acetylene ratio is less than about two, in agreement with the observed initial rate expression. If this ratio is greater than about two, the pressure–time curves are of zero order and the initial rate of pressure fall is given by:

$$-\mathrm{d}P/\mathrm{d}t = k_A P_{H_2} + k_B(P_{H_2} - P^\circ_{H_2})$$

where $P^\circ_{H_2} \simeq 2P_{C_2H_2}$; the temperature-dependence of the rate constants k_A and k_B gives activation energies of respectively 10·3 and 23·8 kcal./mole. The addition of various pressures of hydrogen during an experiment under these conditions leads to faster rates which conform with the above rate expression. If hydrogen is admitted to the reaction vessel before the acetylene, the pressure–time curves generally show two distinct zero-order regions, and the initial rates are proportional to hydrogen pressure over a wide range.

A comparison is made with previous work on similar systems, and possible mechanisms are advanced; physically adsorbed hydrogen molecules may be concerned in the process whose specific rate constant is k_B.

METAL-CATALYSED hydrogenation of acetylene has been the subject of numerous experimental studies, many of which have been described in a recent review.[1] Most of the metals in Group VIII of the periodic classification are efficient for this reaction: but, in addition to the expected products, namely, ethylene and ethane, polymers are formed.[2] The extent of polymerisation varies greatly with the nature of the Group VIII metal, being more marked with iron, cobalt, or nickel than with metals in the palladium and the platinum triad. This variation has been attributed to an effect of the metallic radii.[3] The extent of polymerisation is moreover much less with methylacetylene than with acetylene itself, probably owing to the steric hindrance by the methyl group.[4] The formation of polymers greater than dimers is almost unknown for higher acetylenes.[5]

Other features of interest often met in this system are, first, highly selective production of the corresponding olefin under favourable conditions and, secondly, stereospecific

[1] Bond, in "Catalysis," Vol. III, edited by Emmett, Reinhold Publ. Corp., New York, 1955.
[2] Sheridan, *J.*, 1945, 133.
[3] Sheridan and Reid, *J.*, 1952, 2962.
[4] Bond, *Trans. Faraday Soc.*, 1952, **48**, 651.
[5] Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 77.

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production of a *cis*-olefin when a disubstituted acetylene is hydrogenated. Some results to be presented in Part II will bear on this point.

A further feature of this system, which has received less attention, is the abnormal kinetics. The method of initial rates almost invariably leads to a rate expression of the form:

$$-\mathrm{d}p/\mathrm{d}t = kP_{\mathrm{H_2}}P^{\circ}_{\mathrm{C_2H_2}}$$

although negative orders in acetylene have sometimes been reported. The integrated form of this expression, however, describes the pressure fall as a function of time throughout an experiment in a static system only if the initial hydrogen : acetylene ratio is less than about 2.[6] When this ratio is 2 or more [7] the rate of pressure fall is constant until most of the acetylene has been removed. These statements apply equally to the hydrogenation of acetylene on most of the metals of Group VIII (the exceptions being ruthenium and osmium, which are almost inactive [3]), and to methylacetylene. It is unlikely therefore that the occurrence of the zero-order reaction is connected in any way with polymerisation. No explanation of this effect has yet been proposed.

The present paper describes a detailed study of the kinetics of hydrogenation of acetylene over a nickel–pumice catalyst. This type of catalyst has been used before [2,4,6] and has the merit that it is not poisoned by acetylene as are most unsupported nickel catalysts. All the present work (some 300 runs in all) has been carried out with only two catalyst samples. Particular attention has been paid to studying the conditions under which the zero-order reaction is set up, and to the properties of the reactive layer when this kinetic form obtains.

Experimental

Apparatus.—The apparatus consisted of a standard high-vacuum system with arrangements for purification, storage, and transfer of gases; reactions were carried out in a 100 ml. cylindrical Pyrex vessel. In early experiments, the catalyst granules lay at the bottom of the vessel, but later they were supported on a saucer-shaped spiral of thin glass rod held in the centre of the vessel. Periodic cleaning of the vessel was necessitated by the gradual formation of an involatile liquid polymer.

Temperature Control and Measurement.—The reaction vessel was surrounded by an electrically heated furnace, maintained within $\pm 0{\cdot}1°$. Temperatures were measured with a calibrated chromel–alumel thermocouple.

Reactants and Catalyst.—Hydrogen (British Oxygen Co.) was passed through a bed of platinised asbestos at 200° in an electric furnace, then through a trap immersed in liquid nitrogen.

Acetylene (British Oxygen Co.) was subjected to repeated bulb-to-bulb distillation, with rejection of generous head and tail fractions. In some early experiments, acetylene was prepared by the action of water on calcium carbide, and this behaved identically with the commerical product.

A batch of pumice-supported nickel catalyst containing 9·5% of nickel was prepared by the standard procedure; [4] all the work described in this and the following paper was carried out on two 1 g. samples drawn from it. The first sample (A) was initially reduced with hydrogen *in situ* at 250° for ½ hr., then several times under similar conditions after accidental or intentional exposure to air. 240 runs were performed over this sample during 15 months, after which time it was about five-fold less active than initially; however, some irreversible changes had also occurred, since it did not then exhibit certain kinetic features characteristic of its earlier history. Sample B was reduced with hydrogen *in situ* at 300° for ½ hr.

Analysis.—While most of the work described in this paper relies solely on the interpretation of the observed pressure–time curves, a few product samples were subjected to mass-spectrometric analysis. The instrument has been fully described elsewhere: [8] accelerating voltages of 50 and 12·7 ev were employed. The mass spectrum of each component was measured separately at the appropriate voltage, and the analyses were performed by standard methods.

[6] Sheridan, *J.*, 1944, 373.
[7] de Pauw and Jungers, *Bull. Soc. chim. belges*, 1948, **57**, 618.
[8] Dainton and McElcheran, *Trans. Faraday Soc.*, 1955, **51**, 657.

Results

Effect of Variables on the Form of Pressure–Time Curves.—A large number of experiments between 80° and 110° showed that, in addition to the expected effect of reactant ratio, there was a marked dependence of the form of the pressure–time curves on both the order of addition of the reactants to the reaction vessel and the pretreatment of the catalyst. It is convenient to classify the observed types of pressure–time curves as follows:

Type I: zero-order reaction, the rate being constant up to a pressure fall about equal to the initial acetylene pressure.

Type IIA: a " broken " curve, consisting of two linear portions of different rates.

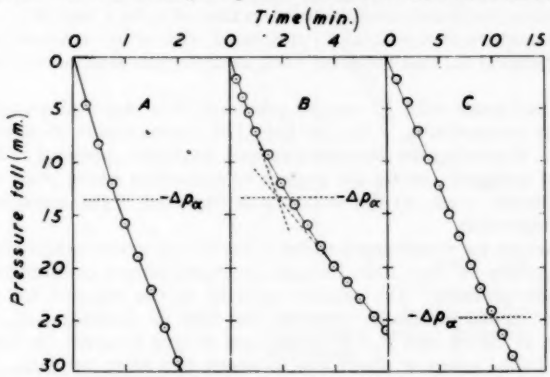
Type IIB: a " broken " curve, consisting of a curved portion (order greater than zero) followed by a linear (zero-order) portion.

Type IIC: as type IIA, but with the break occurring after a greater percentage reaction.

Type III: first-order reaction in hydrogen.

In agreement with previous findings,[4,6] type I curves were only encountered with initial $H_2 : C_2H_2$ ratios greater than about 2, and type III curves with ratios less than about 2. The precise ratio at which the transition from type III to type I occurs will be discussed below. The various type II curves were also only met with when initial $H_2 : C_2H_2$ ratios greater than

FIG. 1. *Examples of pressure–time curves. A, a curve of type* IIA; *B, a curve of type* IIB; *C, a curve of type* IIC. *The initial acetylene pressures were about* 30 *mm. in each case.*



about 2 were used; few experiments were carried out with lower ratios under conditions where type II curves result. Typical examples of the type II curves are shown in Fig. 1; in these curves, the first and the second portion will be referred to respectively as the α- and the β-phase, and the rates as R_α and R_β, the former being the *initial* rate in curves of type IIB. The points of transition between the phases, $-\Delta p_\alpha$, are obtained as shown in Fig. 1. The conditions in the reactive layer which result in a type I curve will be called a type I state; similarly for other types.

When the reactants were admitted to the reaction vessel consecutively, an interval of about 2 min. elapsed between the admissions: such a procedure is equivalent to a 2 min. pretreatment of the catalyst with the first-added reactant before starting the reaction. Type I curves almost invariably resulted when acetylene was admitted first, regardless of the type of curve in the previous experiment, provided only that the initial $H_2 : C_2H_2$ ratio was greater than about two. The only exception was with a freshly reduced catalyst, where the first run showed a type IIA curve; in the second run, a type I curve was obtained by admitting the acetylene 5 min. before the hydrogen, and normal behaviour was then found in succeeding experiments.

Prior addition of hydrogen generally gave curves of type IIB when the initial $H_2 : C_2H_2$ ratio was greater than about two, again regardless of the form of the curve in the previous run. However, pretreatment with hydrogen for 2 min. was insufficient to change the surface state to that of type IIB if the previous run had involved excess of acetylene, and a type I curve resulted instead. It was, however, sufficient to nullify the effect of pretreatment with acetylene for 15 min.

XUM

The types of curve observed when premixed reactants ($H_2 : C_2H_2$ ratio slightly greater than two) were used depended very markedly on the pretreatment to which the catalyst had been subjected. In the reaction of a premixture over a freshly reduced new sample of catalyst, the first two runs gave type IIB curves while the third and subsequent runs gave type IIA curves. This change of behaviour was apparently peculiar to the new sample, as after later reductions following accidental oxidations of the catalyst type IIA curves were immediately obtained with the premixture. When a premixture was used for a series of experiments, the curves were all of type IIA if there had been a hydrogen pretreatment before the first run, or if excess of hydrogen had remained from the previous experiment. However, where there had been an acetylene pretreatment lasting 15 min. or longer (followed by pumping), curves of type I resulted and continued to be given if the interval between runs was not too great. Acetylene pretreatments of up to 3 hr. had no adverse effect on the rate of the following reaction. A run with the premixture following acetylene pretreatment for 10 min gave a curve of type IIC: the period of acetylene pretreatment necessary to convert the surface state from IIA or IIB into I is therefore 10—15 min. at about 100°, and the type IIC curve is regarded as being intermediate between types IIA or IIB and I.

A run in which premixing followed acetylene pretreatment for 17·5 hr. and hydrogen pretreatment for 5 min. gave a type IIA curve, but a further run where the times were respectively 2½ hr. and 1 min. gave a type IIC curve. Hydrogen pretreatment for 1—5 min. is therefore necessary to nullify the effect of a lengthy acetylene pretreatment, and the type IIC curve again denotes a surface state intermediate between that of types I and IIA.

A run with premixture over a catalyst pretreated with either reactant is therefore of the same in type as, or similar to, that obtained when that reactant is admitted first to the reaction vessel.

In series of experiments with (i) various pressures of a standard premixture or (ii) premixtures of various compositions, $-\Delta p_\alpha$ for type IIA curves was 0·34—0·49 times the initial acetylene pressure, depending on temperature and hydrogen pressure. The addition of a further quantity of acetylene during the α-phase of a reaction where prior hydrogen addition was employed increased $-\Delta p_\alpha$ to the value to be expected if the amount added had been present from the beginning.

In the first fourteen runs performed under a variety of initial conditions over the second catalyst sample between 80° and 100°, the rate increased after a pressure fall about equal to the initial acetylene pressure. The relative activity of the catalyst for this second stage declined with time; if the maximum observed fast rate be designated R_γ, the ratio $R_\gamma : R_\beta$ in the case of type II curves and $R_\gamma : R$ in the case of type I curves (R being the zero-order rate) fell from an initial value of about five to about two after ten runs. From a series of experiments performed in close sequence it appeared that R_γ was proportional to the hydrogen pressure at the onset of the acceleration. Similar behaviour has been observed with palladium and platinum catalysts,[4,9,10] and over nickel at lower temperatures,[7] but not in other work with nickel catalysts of the type used here.[4,6] The increased rate is attributable to the faster reduction of the ethylene formed in the first stage of the reaction as compared with that of acetylene, but its occurrence under these conditions is somewhat surprising.

In numerous cases where a type IIA or IIB curve was obtained in a run immediately following or preceding one which gave a type I curve, it was generally found that R_β rather than R_α corresponded to the zero-order rate in the latter case.

Kinetic Behaviour under Type I *and Type* III *Conditions.*—(a) *Orders in hydrogen obtained by the initial-rate method.* Series of experiments were performed to determine the order of the reaction in hydrogen by the initial-rate method, acetylene being admitted first to the reaction vessel, so that curves of types I and III resulted when the initial $H_2 : C_2H_2$ ratios were respectively greater or less than about two. Reaction orders were obtained by using (*a*) differing initial acetylene pressures at the same temperature and (*b*) a constant initial acetylene pressure at varying temperatures, the initial $H_2 : C_2H_2$ ratios lying between about one and eight. A typical set of results is shown in Fig. 2, and all other series gave results of a similar type. The rate–pressure plot is characterised by an inflexion at the point where the initial hydrogen pressure is about twice that of the acetylene pressure, this corresponding approximately to the point at which the pressure–time curves change their form. The rate is directly proportional

[9] Sheridan, *J.*, 1945, 305.
[10] Sheridan, *J.*, 1945, 470.

to hydrogen pressure below the break, and at higher hydrogen pressures it may be assumed that the observed rate is the sum of two separate rates, one of which is directly proportional to hydrogen pressure (a continuation of the first-order process observed at lower pressures), the other being proportional to $(P_{H_2} - P^\circ_{H_2})$ where P_{H_2} is the initial hydrogen pressure and $P^\circ_{H_2}$ the hydrogen pressure at the point where the inflexion occurs, *i.e.*, the threshold pressure for the second reaction. The latter quantity is obtained by interpolation. Thus for type III curves

$$\text{Rate} = k_A P_{H_2}$$

and for type I curves

$$\text{Rate} = k_A P_{H_2} + k_B(P_{H_2} - P^\circ_{H_2})$$

Table 1 summarises the dependence of the ratio k_B/k_A and of $P^\circ_{H_2}$ on the experimental variables: in this Table, $P_{C_2H_2}$ is the mean initial acetylene pressure, individual values being

FIG. 2. *The dependence of initial rate of pressure fall on initial hydrogen pressure at 93·5°; acetylene pressure, 30·5 ± 1·0 mm.*

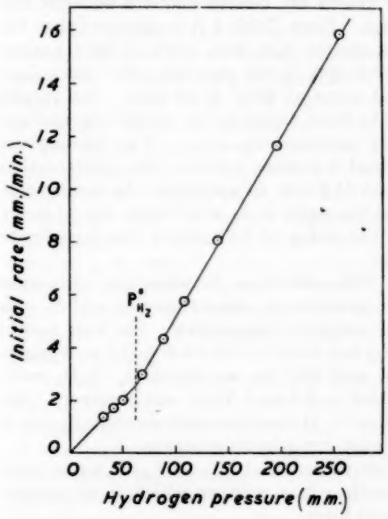
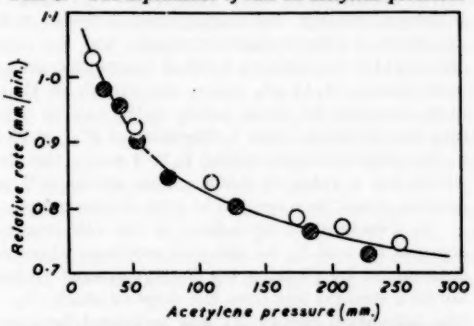


FIG. 3. *The dependence of rate on acetylene pressure.*



○, *Values by the direct method at 85·7°.* ●, *Values by the addition method at 98·2°. See text for further description.*

within 1 mm. of the stated value. At 86°, $P^\circ_{H_2}/P_{C_2H_2}$ is independent of initial acetylene pressure, while k_B/k_A shows a slight but barely significant tendency to increase with increasing acetylene pressure. The quotient $P^\circ_{H_2}/P_{C_2H_2}$ decreases slightly with increasing temperature,

TABLE 1. *The dependence of k_B/k_A and of $P^\circ_{H_2}$ on initial acetylene pressure and temperature.*

Temp.	$P_{C_2H_2}$ (mm.)	$P^\circ_{H_2}$ (mm.)	k_B/k_A *	$P^\circ_{H_2}/P_{C_2H_2}$ †	Temp.	$P_{C_2H_2}$ (mm.)	$P^\circ_{H_2}$ (mm.)	k_B/k_A *	$P^\circ_{H_2}/P_{C_2H_2}$ †
86·0°	14·7	32±1	0·35	2·18	93·5°	30·8	67±2	0·62	2·16
86·0	31·7	70±2	0·41	2·21	110·0	31·2	64±2	0·32	2·05
86·0	60·5	130±4	0·43	2·15					

* ±0·04. † ±0·07.

while k_B/k_A increases very rapidly. The only previous rate measurements made with excess of hydrogen are those by de Pauw and Jungers; [7] using nickel powder at very much lower temperatures, they observed a dependence of rate on hydrogen pressure similar to that described here.

(b) *Order in hydrogen obtained by the addition method.* The implication of the zero-order reaction is that the rate depends solely on the initial partial pressures of reactants and not on

their changing concentrations during the experiment, despite the dependence of rate on hydrogen pressure just described. It might therefore be reasonably expected that the addition of further quantities of either acetylene or hydrogen during a run would have little effect on the rate. Experiments were carried out to test this, and on the contrary it was found that (i) addition of hydrogen led to an increased zero-order rate, and (ii) addition of acetylene led to a decreased rate. These experiments were performed with a premixture whose $H_2 : C_2H_2$ ratio was slightly greater than two, the catalyst having been pretreated with acetylene to establish type I conditions.

A series of experiments was performed at 98·6° with a fixed pressure of a standard premixture to which various hydrogen pressures were added after a fixed pressure fall. By reason of the polymerisation, the rate of total pressure fall is greater than the rate of hydrogen pressure fall by a factor which for the present experimental conditions has been found [11] to be about 1·30. The pressure of the original hydrogen which had not reacted at the time of the addition was calculated with the aid of this factor, and added to the hydrogen pressure which was subsequently admitted. A possible error of ±0·1 on the figure of 1·30 affects this calculation only slightly. The ratio of the rates before and after the addition, R_2/R_1, was then plotted against the total hydrogen pressure after the addition; the points lay closely about a straight line which made an intercept of 28 mm. on the pressure axis. From Table 1 it is apparent that the rate measurements made with initial $H_2 : C_2H_2$ ratios greater than two, when plotted against hydrogen pressure and extrapolated, likewise make intercepts on the pressure axis: the values are however temperature-dependent and the expected value at 98·6° is 29 mm. The results obtained by the addition method therefore correspond to those found by the initial rate method when initial $H_2 : C_2H_2$ ratios are varied, in that they measure $(k_B + k_A)$. One assumption must however be made before k_B/k_A can be determined for these results. By interpolation into the results in Table 1, the value of $P^\circ_{H_2}$ at 98·6° and 33·2 mm. of acetylene (the mean value in the addition experiments) is 70·5 mm.; this defines the value of k_A and hence also of k_B/k_A which has a value of 0·805. This agrees well with the value of 0·78 which the initial-rate method would be expected to give at this temperature.

(c) *Temperature-dependence of the rate constants.* The difference between the activation energies E_B and E_A for the two processes whose rate constants are respectively k_B and k_A was determined by plotting log (k_B/k_A) against reciprocal absolute temperature; the four points lay on a straight line from the slope of which $(E_B - E_A)$ was found to be 13·5 ± 0·1 kcal./mole. The activation energy E_A was measured between 68° and 152° for an initial $H_2 : C_2H_2$ ratio of 1·45, the acetylene being added first. A value of 10·3 ± 0·3 kcal./mole was obtained; this is somewhat lower than the values reported by Sheridan.[2] It therefore follows that E_B has a value of 23·8 ± 0·4 kcal./mole, which is remarkably high for a hydrogenation.

More recent work by Mr. R. S. Mann has however shown that $(E_B - E_A)$ is not a fixed quantity, but varies from one catalyst sample to another in a manner which is at present irreproducible. This aspect of the work will be reported later.

(d) *Orders in acetylene obtained by the initial-rate method.* The order in acetylene was determined by the initial-rate method at 85·7° and a mean initial hydrogen pressure of 51·3 mm.; initial acetylene pressures were between 15 and 254 mm. In the majority of the experiments, the pressure–time curves were of type III, but a plot of initial rate (regardless of the kinetic form of the curve) *versus* acetylene pressure showed no discontinuity of rate in passing from curves of type III to type I. The results are shown in Fig. 3, where the rates are expressed as fractions of the value for an acetylene pressure of 25 mm.: this is to facilitate comparison with results to be described in the next paragraph. The points lie closely about a curve corresponding to an order in acetylene of −0·14.

A second series of experiments was carried out at 92·0° with a mean initial hydrogen pressure of 102·2 mm. and initial acetylene pressures between 15 and 101 mm. In this case the rates (regardless of the kinetic form of the curve) were within error independent of acetylene pressure.

(e) *Orders in acetylene obtained by the addition method.* It has been noted above that addition of acetylene during an experiment giving a type I curve results in a decrease in rate, and several series of experiments (cf. Table 2) were performed to determine the order in acetylene by this method. In the first two and the last two series, the acetylene was added before the hydrogen, while in series III a premixture was used after an acetylene pretreatment. Acetylene pressures within the ranges shown in column 5 were added after the pressure falls given in column 6.

[11] Bond, Ph.D. thesis, Birmingham, 1951.

XUM

In series I, the pressure–time curves both before and after the addition of acetylene were of type III, and the rates were measured from the first-order rate constants after conversion of the observed pressure fall into fall in hydrogen pressure by means of the analytical data.[11] The ratio of the rate constants before and after the addition was plotted against total acetylene pressure after the addition, and the points lay about a curve corresponding to an order in acetylene of −0·19.

TABLE 2. *Summary of the conditions employed and the results obtained in determining orders in acetylene by the addition method.*

Series	Temp.	Initial $H_2 : C_2H_2$	Mean initial P_H, (mm.)	C_2H_2 added (mm.)	$-\Delta p_\alpha$ (mm.)	Order in C_2H_2
I	92·0°	0·99 ± 0·05	50·0	15—157	10·9 ± 0·5	−0·19
II	88·5	1·94 ± 0·11	67·0	12—17	Variable	−0·2
III	98·2	1·98	66·5	29—205	11·3 ± 0·4	−0·14
IV	92·0	2·95 ± 0·10	104·0	19—64	11·8 ± 0·4	0
V	88·0	5·27 ± 0·13	190·0	15—63	11·7 ± 0·7	+0·25

Acetylene added first, except in series III where a premixture was used.

In the second series, the pressure–time curves were presumably initially of type III, but the changes in rate before the additions were insufficient to warrant the determination of rate constants. Initial rates, designated R_1, were therefore measured directly. After the additions, values of k_2 were determined as before and values of R_2 calculated therefrom for a hydrogen pressure of 67 mm.: the change in the hydrogen pressure is thereby allowed for, and the rates R_1 and R_2 are then directly comparable. In the first two experiments, the acetylene was added after pressure falls of respectively 6 and 12 mm. in amounts to give a total acetylene pressure of 43 ± 1 mm. Values of R_2/R_1 were respectively 0·92 and 0·89, *i.e.*, essentially independent of pressure fall. In further experiments, the pressure fall was varied from 6 to 17 mm. and the pressure of added acetylene fixed at 12·5 mm. Values of k_2 were constant within 2%, indicating as expected that the first-order R_2 is proportional to the hydrogen pressure at the time the acetylene is added. When R_2 was corrected to a hydrogen pressure of 67 mm., the ratio R_2/R_1 fell with increasing total acetylene pressure, corresponding to an order in acetylene of about −0·2. The pressure range covered was, however, not large enough to give this value great precision.

In the third series, values of R_1 and R_2 were obtained as described in the last paragraph. The plot of R_2/R_1 *versus* total acetylene pressure is shown in Fig. 3, together with the results obtained by the initial-rate method: the close concordance is strong confirmation of the validity of the addition method of determining reaction orders. Similar experiments at 87·4°, but covering a smaller range of added acetylene pressures, confirmed that the temperature-dependence of the order in acetylene is not great.

In series IV, without allowance for the decrease in hydrogen pressure, the ratio of the rates, R_2/R_1, was unity within 2%, *i.e.*, the order in acetylene was zero. Allowance for the decreased hydrogen pressure at the time of additon changed R_2/R_1 to give a very slightly positive order in acetylene.

In series V, the zero-order rates following the additions were 1·21—1·27 times faster than the initial rates, showing no regular trend with changing total acetylene pressure. Taking the ratio of the rates as unity for an acetylene pressure of 27 mm. gives results corresponding very roughly to an order in acetylene of +0·25.

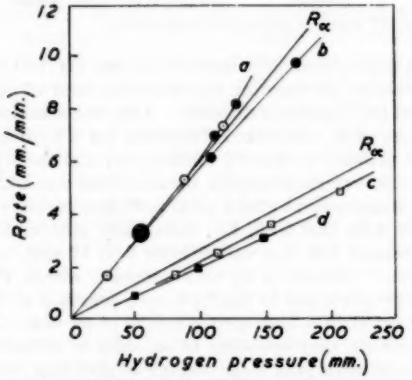
The effect of adding premixed reactants during a type I reaction was studied at 93·5°. Initial $H_2 : C_2H_2$ ratios of 2·12 were used, the acetylene being added first, and variable pressures of a standard premixture ($H_2 : C_2H_2$, 2·10) were added after a pressure fall of 12 mm. Both reactants affected the rate, and it was assumed that the two effects were independent. The action of the added hydrogen was derived from the results described in an earlier section; the ratio $R_2 : R_x$, where R_x is the rate expected simply due to the changed hydrogen pressure, was plotted against total acetylene pressure, and an order in acetylene of about −0·4 was deduced. Since this is much lower than the values found by the other methods, it is likely that the assumption concerning the independence of the effects of the added reactants is not justified.

(f) *Reactant ratio for transition from type I to type III curves.* The initial reactant ratio at which pressure–time curves change from type III to type I has been found to depend on whether the reactants are added singly or in admixture. A premixture having a $H_2 : C_2H_2$

ratio of 1·97 gave a type I curve at 98°, but with prior addition of acetylene a type III curve was obtained with a $H_2 : C_2H_2$ ratio of 2·11 at 93·5° and a type I curve with a ratio of 2·16 at 105°. These results therefore confirm the supposition that the inflexions in the rate–hydrogen pressure plots described above correspond to the point at which the kinetic form of the pressure–time curves change; the transition ratios expected from the hydrogen order plots are respectively 2·16 and 2·08 at 93·5° and 105°.

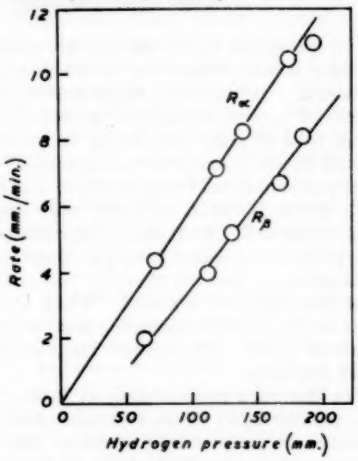
Kinetic Behaviour under Type II Conditions.—(a) *Kinetics under type* IIA *conditions.* As has been described in an earlier section, pressure–time curves showing two distinct zero-order rates were obtained when premixed reactants reacted over a hydrogen-pretreated surface, the inflexion occurring after a pressure-fall equal to obout one-half the initial acetylene pressure. Series of experiments were carried out at temperatures close to 85° and 100°, to determine the

FIG. 4. *The dependence of rates on hydrogen pressure under type* IIA *conditions (premixed reactants).*



a, R_β *relative to* R_α *at* 101·5°; *open circles*, ○, *series* IV; ●, *series* VI. *b*, R_β *relative to* R_α *at* 101·3°, *series* VII. *c*, R_β *relative to* R_α *at* 85·3°, *series* VIII. *d*, R_β *relative to* R_α *at* 85·6, *series* V. (*Individual values of* R_α *are omitted for clarity.*)

FIG. 5. *The dependence of* R_α *and* R_β *on hydrogen pressure under type* IIB *conditions (prior admission of hydrogen) at* 92·0° (*series* II, *Table* 4).



dependence of the two rates on partial-pressure variations at these temperatures. The experiments were of two types: the first employed variable pressures of a standard premixture, so that the partial pressures of both reactants were varied simultaneously, while the second employed pressures of premixtures of various compositions chosen to make the initial pressure of acetylene constant in all cases.

The conditions used in these experiments are detailed in Table 3; where the premixed reactant composition is stated to be fixed, the initial $H_2 : C_2H_2$ ratios were 2·02 ± 0·02. The results are shown graphically in Fig. 4, where values of R_α are plotted against initial hydrogen

TABLE 3. *Summary of conditions employed in studying kinetics by use of premixed reactants.*

	Premixed reactants				
Series	Compn.	Pressure	Temp.	P_{H_2} range (mm.)	$P_{C_2H_2}$ range (mm.)
IV	Fixed	Variable	101·5°	36—142	18—71
VI	,,	,,	101·3	67—158	33—77
VIII	,,	,,	85·3	96—248	47—121
VII	Variable	Fixed $P_{C_2H_2}$,	101·3	67—188	32·9 ± 0·5
V	,,	,,	85·6	81—184	26·0 ± 1·0

pressures, and the corresponding values of R_β against the hydrogen pressure at $-\Delta p_\alpha$, the point at which the rate curves intersect (see Fig. 1). This second hydrogen pressure was obtained by assuming, as before, that the rate of hydrogen removal is 0·77 times that of the

rate of total pressure fall: an error of ±10% on this factor would not affect the results significantly.

The rates R_α are always proportional to initial hydrogen pressure. Series IV and VI (performed respectively over catalyst samples A and B) are in good agreement: in Fig. 4, the rate constant k_α for the latter series has been normalised to fit the value in the former series, and the values of R_β from both series then lie on one curve (curve *a*). The same procedure was then applied to series VII, but the R_β values lie below those for R_α (curve *b*). Similar treatment has been given to the results obtained at 85°, but here both the sets of R_β values (curve *c*, series VIII, and curve *d*, series V) lie below the R_α line.

The results at the higher temperature indicate that for hydrogen pressures less than about 100 mm. R_β is within error proportional to the hydrogen pressure at $-\Delta p_\alpha$: this is more nearly true for series IV and VI than for series VII. Above this pressure, deviations in opposite directions become marked, and increase more rapidly with increasing hydrogen pressure in the case of series IV and VI. The situation at the lower temperature is clearly substantially different.

Values of $-\Delta p_\alpha/P_{C_2H_2}$ (where $P_{C_2H_2}$ is the initial acetylene pressure) vary somewhat with temperature and initial hydrogen pressure: at about 85° values increased smoothly from 0·34 to 0·42 as the hydrogen pressure rose from 60 to 160 mm., while at about 100° they increased from 0·43 to 0·49 in the same hydrogen-pressure range.

(b) *Kinetics under type* IIB *conditions.* Series of experiments at 81·5°, 92·0°, and 104·6° employed a fixed initial pressure of acetylene (~30 mm.) and a variable pressure of hydrogen, the latter being admitted to the reaction vessel before the acetylene. Pressure–time curves were of type IIB. The results of a typical series of experiments are shown in Fig. 5, where R_α (obtained as described earlier) is plotted against the initial hydrogen pressure, and R_β against the hydrogen pressure at $-\Delta p_\alpha$, the point at which the extrapolated rate curves intersect (see Fig. 1). This second hydrogen pressure was estimated in the usual manner. Since $-\Delta p_\alpha$ is approximately constant in all these experiments, an error in the factor of 0·77 will lead to a

TABLE 4. *Kinetic results obtained with prior addition of hydrogen.*

Series	Temp.	P_{H_2} (mm.)	$P_{C_2H_2}$ (mm.)	k_α (min.$^{-1}$)	Mean $-\Delta P_\alpha$	k_β (min.$^{-1}$)	P'_{H_2} (mm.)	$k_\alpha : k_\beta$
I	81·5°	75—226	32·0 ± 1·0	0·0531	12·5	0·0435	25	1·220
II	92·0	73—197	32·3 ± 1·3	0·0587	11·0	0·0498	27	1·180
III	104·6	74—153	32·5 ± 1·5	0·0991	12·0	0·0860	28	1·151

constant error in the calculated hydrogen pressure; this will affect only the lateral position of the R_β–hydrogen pressure line (and only slightly), and not the slope. The series at the other temperatures gave results of the same form. Table 4 gives details of these experiments. The equations relating the quantities in the Table are $R_\alpha = p_\alpha P_{H_2}$ and $R_\beta = k_\beta(P_{H_2} - P'_{H_2})$, but the second equation is not valid at hydrogen pressures less than about 70 mm. The ratio $k_\alpha : k_\beta$ is seen to be only very slightly temperature-dependent. In these experiments, values of $-\Delta p_\alpha/P_{C_2H_2}$ (which cannot be determined with great accuracy) are rather smaller than in experiments with premixed reactants. Individual values range between 0·33 and 0·40, but are too scattered to reveal any dependence on initial hydrogen pressure: mean values at the three temperatures show no regular dependence on temperature.

Selectivity.—The products of a few runs were subjected to mass-spectrometry, to determine the ethylene : ethane ratio. The results are in Table 5; the analyses were performed after pressure falls equal to the initial acetylene pressure. The degree of selectivity is here expressed as ethylene yield divided by the sum of the ethylene and the ethane yield. Sheridan's results [2] obtained at the same temperature are included in the Table.

TABLE 5. *Dependence of the degree of selectivity on hydrogen pressure, at* 99·0° ± 0·5°.

Run	$P_{C_2H_2}$ (mm.)	P_{H_2} (mm.)	Selectivity	Reference	Run	$P_{C_2H_2}$ (mm.)	P_{H_2} (mm.)	Selectivity	Reference
A-231	38·2	52·0	0·866	This work	B-46	35·0	124·8 *	0·902	This work
A-232	35·0	124·5	0·854	,,	—	200	200 *	0·890	Ref. 2
B-45	37·9	131·0	0·864	,,	—	200	400 *	0·846	,,

* Hydrogen added first to the reaction vessel.

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The selectivities found when the normal order of addition is followed agree well with Sheridan's values, although he employed the reverse order of addition. They are independent of hydrogen pressure. There is evidence that in this work prior addition of hydrogen to the reaction vessel results in a somewhat higher selectivity (run B-46); the age of the catalyst sample is apparently irrelevant (compare runs A-232 and B-46).

Reactions between Adsorbed and Gaseous Reactants.—Experiments were conducted to determine the products of the reactions between (i) gaseous hydrogen and adsorbed acetylene, and (ii) gaseous acetylene and adsorbed hydrogen. These experiments were expected to yield information concerning the species adsorbed on the surface under the various conditions giving rise to the various forms of pressure–time curves.

The procedure was as follows: Catalyst sample A was treated with acetylene for 20 hr. at 88·6° and pumped at this temperature for 3 hr., after which time the pressure in the reaction vessel was below 10^{-6} mm.; 155 mm. of hydrogen were added immediately the pumping was stopped, and portions of the gas removed for analysis by mass-spectrometry after 1 and 12 min. (run A-76). 18 hr. later the remainder of the hydrogen was evacuated at 88·6°, the pumping being continued for 2½ hr., after which time a hard vacuum was obtained. 127 mm. of acetylene were then admitted, and samples removed for analysis after 1 and 12 min. (run A-77). The cycle of operations used in run A-76 was then repeated, the acetylene added in run A-77 effecting the pretreatment: 89 mm. of hydrogen were used in this experiment (run A-78).

The samples from runs 76 and 78 contained chiefly hydrogen, with small amounts of hydrocarbons and larger amounts of nitrogen (resulting from the original air content of the hydrogen): the analyses were therefore only semiquantitative. In neither case did the 1-min. samples contain any acetylene, only ethylene being detected: the 12-min. samples both contained acetylene (about twice as much in run 76 as in run 78), and ethylene in the same concentration as in the samples taken after 1 min. The ethylene concentration lay between the two 12-min. acetylene concentrations. No ethane was detected in any sample. These results suggest that, on addition of hydrogen, part of the adsorbed acetylene is rapidly hydrogenated to ethylene and part is slowly displaced. The fact that the 12-min. sample from run 76 contained more acetylene than that from run 78, and that a higher hydrogen pressure was used in the former case, might mean that the rate of displacement increases with increasing hydrogen pressure. It is therefore possible that the displacement was not complete even after 12 min. The failure of the ethylene and acetylene to be further reduced is probably explained by saying that their chances of adsorption in an overwhelmingly predominant hydrogen atmosphere were negligible.

The sample from run 77 was chiefly acetylene, but ethylene was detected and its concentration did not change with time: no ethane was found. Work to be described in Part II provides evidence that the reaction is not simply the one-stage addition of two adsorbed hydrogen atoms to an acetylene molecule.

Discussion

It must now be recognised that an unsuspected number of variables affect the kinetics (and therefore the mechanisms) of hydrogenation reactions over supported metal catalysts. Those made apparent by the present work are: (1) the ratio of the partial pressures of the reactants, (2) the order of their addition to the reaction vessel, and (3) the pretreatment of the catalyst. Comparison of this work with an earlier study on nominally the same system indicates a fourth, namely, (4) the method of preparing the catalyst. Thus Sheridan [2,6] consistently obtained type I curves although adding hydrogen to his reaction vessel before the acetylene; he reduced his catalysts in hydrogen containing ethanol vapour at about 400°. This order of addition when used here always gave type IIB curves. More recent work, to be reported later, suggests that the above list is by no means exhaustive. Any detailed interpretation of the kinetics in a given system should therefore be limited to that system, and may not have wider validity. With this reservation, the results presented above will be discussed.

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The Shapes of Pressure–Time Curves.—The results make it clear that the nature and concentrations of the species in the reactive layer vary with experimental conditions, and that changes in their concentrations as the composition of the ambient gas mixture is altered are not always instantaneous. It may be assumed as a starting point that pretreatment of the surface by acetylene results in the formation of a complete chemisorbed layer of this species. Subsequent addition of hydrogen results in a type I or type III curve (depending on the initial hydrogen : acetylene ratio), and it is therefore thought that in a type I or type III surface state the reactive layer is initially poor in hydrogen, and that this state of affairs is maintained throughout the reaction. The principal species in the reactive layer may be adsorbed acetylene and adsorbed vinyl radicals.

On the other hand, it is believed that pressure–time curves of types IIA and IIB result when the reactive layer is initially richer in hydrogen. This additional hydrogen may exist in the form of atoms or more probably combined with acetylene as vinyl radicals. The time required to convert a type I surface state into a type IIA or IIB state depends in some measure on the length of the acetylene pretreatment, and on the procedure in the test run. The situation is roughly the same whether the hydrogen treatment is followed by addition of acetylene (prior hydrogen addition, curve type IIB) or by evacuation of the hydrogen before the addition of premixed reactants (curve type IIA). In the former case, hydrogen pretreatment for 2 min. is sufficient if the foregoing acetylene pretreatment has been short, while in the latter case a hydrogen treatment of 1—5 min. nullifies the effect of lengthy acetylene pretreatment. The times required for the hydrogen concentration in the reactive layer to build up to those values which give rise to curves of type IIA and IIB are therefore appreciable.

As a general principle it is proposed that the kinetic form of the pressure–time curve depends on the nature and especially on the concentrations of the species in the reactive layer at the moment the massive reaction begins; and that if the initial surface state is near its equilibrium state, a steady rate results; and that if it is not the rate alters (from R_α to R_β) as the surface adjusts itself towards the equilibrium state.

Consideration may now be briefly given to the reconversion of a type IIA orIIB surface state into a type I state. Acetylene pretreatment for 2 min. is sufficient to effect this change if the hydrogen is then added to the acetylene to start the massive reaction, whereas a longer acetylene pretreatment (10—15 min.) is required if the acetylene is pumped off and premixed reactants added to effect the massive reaction. The following qualitative explanation can be advanced. The 10—15 min. period is required to form an adsorbed acetylene layer which is stable to pumping: if evacuation is started after a shorter time, some weakly adsorbed acetylene is removed, leaving some surface vacancies which can interact with the hydrogen in the premixture, yielding a surface state giving a type IIC pressure–time curve. If however the acetylene is not pumped off, but hydrogen is added to start the reaction, the hydrogen is presented with a coherent layer of adsorbed acetylene and a type I curve results. This explanation implies either surface heterogeneity (for which there is other evidence) or a relatively slow migration of acetylene from a weakly bound state to a more strongly bound state.[12]

Further evidence supporting these concepts comes from studying the reaction between one gaseous and one adsorbed reactant. If one assumes again that prolonged exposure of the surface to acetylene leads to a complete layer of chemisorbed acetylene, the reaction of gaseous hydrogen with adsorbed acetylene converts a type I surface state into a type IIA or IIB state. The appearance first of ethylene and then of acetylene shows that there must be appreciable but not complete coverage of the surface by chemisorbed hydrogen (or vinyl radicals) in the type II state. The fact that in this process the adsorbed acetylene suffers either desorption or hydrogenation is evidence for an energetically heterogeneous surface.

Further, that the reaction of gaseous acetylene with adsorbed hydrogen leads to the *rapid* formation of ethylene shows that the adsorbed hydrogen layer is quickly replaced

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by an adsorbed acetylene layer, and this lends weight to the suggestion that the concentration of adsorbed hydrogen in the type I state is low.

Kinetics under Type I *and Type* III *Conditions.*—A change in the form of pressure–time curves as the ratio of the partial pressures of the reactants is changed has been found previously,[4, 6] although its significance has not been discussed. The most difficult observation to interpret (and the one which probably contains the key to the problem) is the zero-order kinetics found when the initial hydrogen : acetylene ratio is greater than about two. Disagreement between kinetic expressions derived from initial-rate measurements and those derived by analysing the course of the reaction is by no means uncommon in heterogeneous catalysis; a number of such cases have been discussed theoretically by Thon and Taylor,[13] who suggested the importance of surface chain reactions. They proposed that in the initial stages of a reaction a chain-carrying intermediate determines the rate; if this maintains its concentration through the reaction, the later kinetics will be of zero order, but if its concentration declines during the reaction, the later kinetics will be complex and in disagreement with the initial-rate expression. In the limit, if the chain reaction is not sustained, the integrated form of the initial-rate expression will describe the change in rate throughout the reaction.

This concept is however not without its difficulties, especially when applied to the interpretation of a zero-order rate. First, a stationary concentration of intermediates must be maintained throughout the reaction, and it is difficult to see why the intermediate-forming process should cease after the early stages of the reaction. All conceivable combinations of initiation, propagation, and termination processes lead to a concentration of intermediates which may be instantaneously constant but which nevertheless must respond to changes in the pressures of the reactants and thus change through the reaction. Secondly, the product-forming step involves at least one reactant whose pressure will decline through the reaction, and a zero-order rate can only result if the stationary concentration of intermediate is inversely proportional to the pressure of that reactant which reacts with it to form the product. Application of this concept to the present system has not proved fruitful.

The situation in the case of type III pressure–time curves is relatively straightforward: the integrated form of the initial-rate expression (neglecting the slightly negative order in acetylene) describes the change of rate during any reaction. For type I pressure–time curves, the situation is more complex, for they have three characteristics which require interpretation. (1) The rate is constant and thus apparently not responsive to *slow* changes in the gas composition. (2) *Abrupt* changes in the partial pressure of either reactant do affect the rate in a manner which reflects the initial-rate dependence on gas pressures. (3) The initial-rate expression is complex and suggests that the transition in the form of the pressure–time curves from type III to type I is caused by the opening of a second reaction path.

In constructing a tractable reaction mechanism, certain simplifications must be introduced and these must be justified at the outset. It is proposed to set up a reaction scheme leading only to the production of ethylene. Neglect of processes leading to ethane in the early stages of the reaction (*i.e.*, before the acetylene pressure has fallen to near zero) is justified by the observation (Table 5) that the selectivity does not change very significantly within the range of experimental conditions to which this discussion relates. Thus the rate of pressure fall due to the further hydrogenation of ethylene will account for an approximately constant fraction of the total rate. The neglect of steps leading to polymers may be more serious, but there are good grounds for believing that the kinetics of such processes are similar to, if not identical with, those producing ethylene and ethane.[2, 6] For the present purpose it therefore suffices to assume that the observed rate of pressure fall is proportional to the rate of ethylene formation.

[12] Dowden, in "Chemisorption," edited by Garner, Butterworths, London, 1957.
[13] Thon and Taylor, *J. Amer. Chem. Soc.*, 1953, **75**, 2747.

The initial adsorption processes (bold type indicates adsorbed species),

$$H_2 \underset{k'_H}{\overset{k_H}{\rightleftharpoons}} 2\mathbf{H} \text{ and } C_2H_2 \underset{k'_C}{\overset{k_C}{\rightleftharpoons}} \mathbf{C_2H_2}$$

are assumed to be followed by

$$\mathbf{H} + \mathbf{C_2H_2} \underset{k'_1}{\overset{k_1}{\rightleftharpoons}} \mathbf{C_2H_3} \quad \ldots\ldots\ (1)$$

the relative magnitudes of k_1 and k'_1 being such that the equilibrium lies far to the right and the concentration of adsorbed hydrogen atoms sufficiently low to render unnecessary the consideration of other possible processes involving them. Ethylene is taken to be formed in the process

$$2\mathbf{C_2H_3} \xrightarrow{k_2} C_2H_4 + \mathbf{C_2H_2} \quad \ldots\ldots\ (2)$$

If competitive adsorption of the two reactants is assumed, then:

$$[\mathbf{H}] = \frac{b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}{1 + b_C P_{C_2H_2} + b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}$$

and

$$[\mathbf{C_2H_2}] = \frac{b_C P_{C_2H_2}}{1 + b_C P_{C_2H_2} + b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}$$

where $b_H = k_H/k'_H$ and $b_C = k_C/k'_C$. The hydrogen atoms are then rapidly converted into vinyl radicals whose stationary concentration is given by:

$$[\mathbf{C_2H_3}] = \frac{k_1}{k'_1}[\mathbf{C_2H_2}] \frac{b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}{1 + b_C P_{C_2H_2} + b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}$$

on the permissible assumption that $k'_1 \gg k_2$. If $[\mathbf{C_2H_2}]$ is set equal to unity (*i.e.*, a low concentration of vinyl radicals is assumed), the rate of production of ethylene, step 2 being taken as the only relevant process, is given by:

$$\begin{aligned} dp_{C_2H_4}/dt &= k_2[\mathbf{C_2H_3}]^2 \\ &= k_2\left(\frac{k_1}{k'_1}\right)^2 \cdot \frac{b_H P_{H_2}}{(1 + b_C P_{C_2H_2} + b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}})^2} \quad \ldots\ (A) \end{aligned}$$

If as is likely $b_H \gg b_C$, this expression gives a rate which is proportional to hydrogen pressure and to a small negative power of acetylene pressure (depending on the magnitude of b_C), in agreement with observation under type III conditions.

An alternative and essentially equivalent treatment is to suppose that the hydrogen is introduced into the reactive layer by the mechanism:

$$2\mathbf{C_2H_2} + H_2 \underset{k'_3}{\overset{k_3}{\rightleftharpoons}} 2\mathbf{C_2H_3} \quad \ldots\ldots\ (3)$$

whence

$$\left(\frac{k_3}{k'_3}\right)^{\frac{1}{2}} \equiv \frac{k_1}{k'_1} \cdot \frac{b_H^{\frac{1}{2}}}{1 + b_C P_{C_2H_2} + b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}}$$

If the terms $b_C P_{C_2H_2}$ and $b_H^{\frac{1}{2}} P_{H_2}^{\frac{1}{2}}$ are each much less than unity,

then

$$\left(\frac{k_3}{k'_3}\right)^{\frac{1}{2}} \equiv \frac{k_1}{k'_1}\left(\frac{k_H}{k'_H}\right)^{\frac{1}{2}}$$

The stationary concentration of vinyl radicals is then given by:

$$[\mathbf{C_2H_3}] = \left(\frac{k_3}{k'_3}\right)^{\frac{1}{2}} \cdot P_{H_2}^{\frac{1}{2}} \cdot [\mathbf{C_2H_2}]$$

and equating $[\mathbf{C_2H_2}]$ to unity as before gives

$$\frac{dp_{C_2H_4}}{dt} = \frac{k_2 k_3}{k'_3} \cdot P_{H_2}$$

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This treatment thus also gives a rate which is of the first order in hydrogen, but owing to the assumption concerning the size of the term $b_C P_{C_2H_2}$ it does not allow a negative order in acetylene.

With reference to the kinetics under type I conditions, the overall rate is a function of hydrogen pressure, while for a given hydrogen pressure the relative contributions of the two mechanisms depend on the acetylene pressure. Now the orders of reaction show that acetylene is much more strongly adsorbed than hydrogen, so that it is unlikely that the concentration of chemisorbed acetylene is the relevant variable: the onset of the second mechanism may, however, be determined by the reactant concentrations in a physically adsorbed layer above the reactant layer. Owing to the substantially higher " boiling " point of acetylene, this reactant will be much more strongly physically adsorbed than hydrogen, and it is therefore proposed that the second mechanism comes into operation when the hydrogen : acetylene ratio in the gas phase exceeds a certain critical value which is sufficient to secure the initial entry of the hydrogen into the second layer. The concentration of molecular hydrogen in this layer, designated $[H_2^*]$, is then given by:

$$[H_2^*] = k[P_{H_2} - P^\circ_{H_2}] \doteqdot k[P_{H_2} - 2P_{C_2H_2}] \quad . \quad . \quad . \quad . \quad (B)$$

The required rate expression is most readily obtained if it is supposed that this hydrogen can add directly to an acetylene molecule, *viz.*:

$$C_2H_2 + \overset{H_2}{\vdots} \xrightarrow{k_4} C_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

When the alternative method for the derivation of the type I kinetics is used, the total initial rate becomes, on equation of $[C_2H_2]$ to unity as before:

$$dp_{C_2H_2}/dt = \frac{k_2k_3}{k_2 + k'_3} \cdot P_{H_2} + k_4[H_2^*]$$

which when combined with equation B quantitatively describes the dependence of rate on hydrogen pressure over a wide range of conditions.

We cannot explain the apparent dependence of the order in acetylene on hydrogen pressure; Table 2 reveals that zero orders (or greater) in acetylene are recorded under conditions where the initial hydrogen : acetylene ratio is generally greater than about two (except in Series IV), and that negative orders relate to conditions where the initial reactant ratio is less than about two. Now negative orders in acetylene under type III conditions have already been qualitatively interpreted (equation *A*), and it is suggested that step 4 has in fact an order in acetylene which is positive to just the same extent as the order for step 2 is negative. The effects therefore tend to cancel when steps 2 and 4 make approximately equal contributions to the total rate, and the overall order in acetylene may even become slightly positive when step 4 predominates over step 2. No more quantitative treatment is justified at present.

It is now necessary to enquire into the cause of the zero-order course rate. From equation *B*, the quantity $[H_2^*]$ increases proportionately as P_{H_2} decreases, and these effects tend to cancel; and for the specific case where $k_4 = k_2k_3/(k_2 + k'_3)$, the cancellation is complete and a zero-order course rate should result. The fact that constant rates are observed even where this equality does not hold even approximately indicates that additional factors are operating. For example, when $k_4 = k_2k_3/(k_2 + k'_3)$ an increase in rate would be predicted, and its non-occurrence may be due to a decrease in the rate of step 4 through the decreasing acetylene pressure. Similarly, when the reverse holds, the expected decrease in rate may be partly off-set by the negative order in acetylene of steps 1 and 2.

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The effects observed when either reactant is added during a type I experiment are now readily explicable. The addition of hydrogen increases both P_{H_2} and, disproportionately, $[H_2^*]$, and hence from equation B the overall rate. This equation relates equally to initial hydrogen pressures and to hydrogen pressures throughout a run, whether additional hydrogen has been introduced or not. It is thus inevitable that consistency should be obtained between reaction orders determined by the initial-rate and " addition " methods. The same arguments apply *mutatis mutandis* to variation of acetylene pressure.

Kinetics under Type II *Conditions.*—No comprehensive interpretation of all the various features associated with the kinetic measurements under type II conditions is possible at present. The experiments covered a much smaller range than that employed in studying type I and type III conditions, and further work is called for. For premixed reactants (type IIA state, Table 3 and Fig. 4), the initial rate R_α has been shown to be proportional to hydrogen pressure and essentially independent of acetylene pressure, the peculiar hydrogen-pressure dependence characteristic of type I and type III states not being exhibited. It follows that the surface is still effectively saturated with acetylene and that the direct-addition mechanism (step 4) does not occur in these circumstances. The same is true of experiments involving prior addition of hydrogen, save that here no experiments were performed to determine the order in acetylene.

An even more puzzling feature of the type II state is that there is no return to the " equilibrium state " (*i.e.*, that supposed to exist when acetylene is added before the hydrogen) during the course of the experiment. The hydrogen-pressure dependence of the β-rates is in neither case the same as the dependence of the zero-order rate under type I conditions. The absence of the direct-addition mechanism in the β-phases also is therefore inferred: for example, the temperature dependence of k_β (Table 4) corresponds to an E_β of 7—8 kcal./mole as against about 23 kcal./mole for the zero-order rates. The apparent equivalence of R_β and the zero-order rate must therefore be fortuitous.

Although it is felt that an explanation can most profitably be sought in terms of a varying initial hydrogen content of the reactive layer, a number of as yet unappreciated factors are at work, and an interpretation of the results in terms of detailed mechanisms must await the conclusion of further work.

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554. *The Kinetics of the Decomposition of the Addition Compounds formed by Sodium Bisulphite and a Series of Aldehydes and Ketones. Part I.*

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In aqueous solution sodium bisulphite reacts reversibly with an aldehyde or ketone to form an addition compound. The kinetics of the decomposition of a series of such compounds have been studied. The reaction is of the first order with respect to the addition compound, and the rate increases with the pH of the solution. The energy of activation and the frequency factor are reported for each compound, the series as a whole being built up by progressive substitution of formaldehyde, the simplest reactant. The results indicate that the rate of the reaction is influenced very little by electronic effects but that two steric effects are in operation. One of these effects operates by reducing the activation energy with increasing bulk of substituent whereas the other acts in the opposite sense. In both cases there is evidence for an accompanying change in frequency factor tending to offset, in some measure, the change in rate which the change in activation energy would otherwise cause.

Stewart and Donnally [1] observed that in acid solution the decomposition in presence of iodine of the addition compound formed by sodium bisulphite and benzaldehyde is of the first order with respect to the addition compound and independent of the amount of iodine present. The iodine simply oxidises the free bisulphite as it is formed and allows the decomposition to proceed to completion instead of to the equilibrium:

$$\text{Addition Compound} \rightleftharpoons \text{Free Bisulphite} + \text{Free Aldehyde}$$

The present investigation of a series of these addition compounds was designed to yield information about the influence of structure on reactivity.

Experimental

The aldehydes and ketones came from a variety of sources. Liquids were purified by distillation under suitable pressures, and certain of the solids were recrystallised, although the preparation of a bisulphite compound itself constitutes purification. *o*-Propoxybenzaldehyde was prepared by a variant of Buu-Hoï's method for the preparation of *o*-butoxybenzaldehyde.[2] 18 g. of rapidly crushed potassium hydroxide pellets were added to 26 ml. of salicylaldehyde and 70 ml. of propyl iodide (both freshly distilled), and the mixture was gently refluxed for 15 hr. with constant stirring. When cool the mixture was extracted with dry ether, which was later removed by gentle warming. The remaining propyl iodide was distilled off at 8 mm. and the product was fractionated through a short column at <1 mm.

The procedure for the preparation of a bisulphite addition compound was as follows.[3] A suitable volume of saturated aqueous sodium bisulphite was prepared at room temperature and 70% of its own volume of ethanol was added. Enough water to clear the solution was then added with constant stirring, followed by the aldehyde or ketone in suitable amount relative to the volume of bisulphite solution. The solution became hot and the addition compound was precipitated at once or on cooling. Stirring was continued for 30 min. after which the precipitate was filtered off, washed with a little alcohol, and dried in a vacuum desiccator ($CaCl_2$) for at least 3 days. The basic procedure was varied when necessary: chloral hydrate, for example, was dissolved in a very little hot water before addition of bisulphite solution, and in the preparation of the acetaldehyde compound it was best to omit the alcohol in the first

[1] Stewart and Donnally, *J. Amer. Chem. Soc.*, 1932, **54**, 2333, 3555, 3559.
[2] Buu-Hoï, *Compt. rend.*, 1945, **221**, 202.
[3] Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green and Co. Ltd., London, 1948, p. 340.

stage and precipitate the product finally by a large excess of alcohol. The addition compounds obtained by this method may contain some free bisulphite or perhaps a little aldehyde if this is solid at room temperature. It will be shown that these impurities would not interfere with the rate determinations.

The rate of the reaction could be measured over the range where the pseudo-first order rate constant, k, was between 10^{-1} sec.$^{-1}$ and 10^{-5} sec.$^{-1}$. Since the bisulphite ions liberated in the decomposition are oxidised to bisulphate ions by iodine, reaction mixtures of high buffer capacity are needed to maintain the correct pH. Rather concentrated buffers were therefore used and the reaction mixtures were only 0·01 molar with respect to the addition compound. The buffer solutions were made up as follows, reagents of "AnalaR" quality being used as in the preparation of iodine solutions: for pH 3, 0·1200M in potassium hydrogen phthalate and 0·04878M in hydrochloric acid; for pH 5, 0·1192M in sodium acetate and 0·04972M in acetic acid. The pH was measured with a glass electrode before, during, and after trial runs at each pH and the buffer solutions were found to be satisfactory. At pH 5 the buffer showed signs of failing as the reaction proceeded but not enough for rate constants based on the early part of the reaction to be seriously in error.

Activation energies were calculated by the method of least squares from rate constants at five or six different temperatures. For solutions of pH 3 the range was generally from about 20° to 40° and at pH 5 either from 5° to 25° or from 20° to 40°. These temperature ranges are such that no significant change in pH was produced by a change in dissociation constant of the weak acid used in the buffer, the dissociation constants of acetic acid and phthalic acid varying with temperature in such a way that the pH change is less than 0·04 unit over the whole range of either buffer used in the experiments.[4] The only possible "buffer error" is therefore a systematic one because the actual pH might have been a little above or a little below that indicated by the glass electrode. This error, however, would be the same for all compounds studied.

The rate of reaction was measured by the following method. 50 ml. of the appropriate buffer solution and 1 ml. of starch indicator were placed in a 250-ml. conical flask and immersed in a thermostat for at least 30 min. before the start of the run. At room temperature or above water thermostats maintaining the temperature constant to within $\pm$0·05° were used and below room temperature a refrigerated thermostat was used giving control to within $\pm$0·15°. Enough of the bisulphite addition compound to make 50 ml. of approximately 0·01M solution was weighed accurately in a small wide-mouthed glass tube and a suitably small volume, say 0·5 ml., of approximately 0·01M-iodine solution was added to the mixture. The bisulphite compound was then added together with the containing tube, time "zero" being generally taken to be the moment of addition since the addition compounds dissolved in a few seconds. The time at which the blue colour disappeared was noted and gave the time for an amount of reaction corresponding to the iodine first added. A further small volume of iodine was at once added and the sequence was repeated. The amount present had no effect at all on the rate of the reaction, the iodine simply removing one product as fast as it was formed. In all experiments below room temperature the iodine solutions were chilled to the temperature of the thermostat. The reaction vessels were always kept stoppered between additions to prevent loss of iodine as vapour.

"End-points" were obtained by the following procedure. In buffer solution of pH 6·7 (42·981 g. of disodium hydrogen phosphate dodecahydrate and 10·887 g. of potassium dihydrogen phosphate per litre of solution) the rate of decomposition of every addition compound studied was extremely great and it was therefore possible to titrate small weighed amounts in 50 ml. of buffer against iodine solution. Several small amounts of each compound (greater, less, and equal to the amount required to make 50 ml. of 0·01M-solution) were weighed out and titrated with iodine in this way at pH 6·7. The results gave the linear relations between volume of iodine required for complete reaction and weight of bisulphite compound used. All end-point volumes for the compound could then be read off the graph since the amount used in each run was accurately known. Both the calibration and the corresponding runs were done on the same day with the same iodine solution. The vast majority of the aldehydes and ketones liberated by the decomposition of the addition compounds reacted much too slowly with iodine for their own secondary reaction with it to be a source of error in the rate measurements, but

[4] Robinson and Stokes, "Electrolyte Solutions," Butterworths Scientific Publications, London, 1955, p. 496.

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calibration titrations with the acetaldehyde compound had to be carried out rather quickly, slow fading after the first end-point being ignored. With propionaldehyde it was impossible for this reason to do more than estimate the rate very roughly at pH 3.

The presence of a little free carbonyl compound has no effect on the rate of reaction. Traces of bisulphite are easily allowed for as follows. Free bisulphite reacts instantaneously with iodine at any pH and therefore makes its presence known by giving the reaction a very fast start. One pilot run for each compound is sufficient to establish the amount, if any, of this " fast reaction " corresponding to a known weight of addition compound and in all subsequent runs the first addition of iodine can be augmented by the amount required to neutralise the free bisulphite. The iodine thus added is subtracted from the end-point volume and the time zero is moved to the first disappearance of the blue colour.

Results

A pseudo-unimolecular rate constant, k (sec.$^{-1}$), was calculated for each run from the good first-order plots given by the experimental data, and reproducibility was satisfactory. Table 1 gives the principal experimental data for all the compounds studied; k and A are in sec.$^{-1}$. The general results may be summarised as follows.

Table 1. *Decomposition of bisulphite addition compounds in aqueous solution at 20°.*

	pH 3				pH 5			
Compound	5 + $\log_{10} k$	E (cal.)	ΔE (cal.)	$\log_{10} A$	5 + $\log_{10} k$	E (cal.)	ΔE (cal.)	$\log_{10} A$
PhCHO	1·19	17,750	—	9·44	2·89	14,550	—	8·77
o-Cl-	1·20	17,850	+ 100	9·48	—	—	—	—
o-NO_2-	1·15	18,200	+ 450	9·70	—	—	—	—
o-MeO-	1·07	19,050	+1300	10·2	2·74	16,150	+1600	9·79
o-EtO-	0·98	19,250	+1500	10·3	2·67	17,000	+2450	10·4
o-PrO-	0·95	19,700	+1950	10·6	2·56	18,000	+3450	11·0
p-NO_2-	1·25	17,550	− 200	9·33	—	—	—	—
p-Cl-	1·28	17,550	− 200	9·37	2·94	14,250	− 300	8·57
p-Me-	1·28	17,850	+ 100	9·59	3·05	16,500	+1950	10·3
m-NO_2-	1·28	18,100	+ 350	9·76	—	—	—	—
p-Me_2N-	1·32	19,850	+2100	11·1	—	—	—	—
p-MeO-	1·41	17,150	− 600	9·19	3·16	15,550	+1000	9·77
p-HO-	1·43	17,850	+ 100	9·73	3·24	17,800	+3250	11·5
o-HO-	2·10	15,300	−2450	8·53	3·91	15,350	+ 800	10·4
CCl_3·CHO	2·55	19,600	+1850	12·1	—	—	—	—
$COMe_2$	0·82	18,850	+1100	9·87	2·69	19,600	+5050	12·3
$CH_2<[CH_2]_4>CO$	0·45	20,950	+3200	11·0	2·12	17,850	+3300	10·4
EtCHO	≈0·1	—	—	—	—	—	—	—
MeCHO	−0·46	21,650	+3900	10·7	1·40	19,400	+4850	10·9
HCHO	—	—	—	—	−0·26	22,350	+7800	11·4

(1) The reaction is invariably faster at the higher pH and the activation energy is generally lower. A temperature of 20° has been selected for comparing rates and the benzaldehyde compound is used as the reference standard. At each pH $\Delta \log k$ is calculated for all compounds relative to benzaldehyde and the results appear in Fig. 1. It is immediately obvious that all manifestations of substituent effects are pH independent or nearly so.

(2) In view of the inherent uncertainty about the precise absolute value of the pH in the buffer solutions it is not possible to do more than estimate the order of the reaction with respect to hydroxyl-ion concentration. It would, however, appear that the true order is less than, or equal to, but never greater than unity.

(3) Figs. 2 and 3 show the result of plotting $\log_{10} k$ against energy of activation, E (kcal.), at pH 3 and at pH 5, respectively. (Several compounds were studied at one pH only, generally the lower one.) The lines are of slope $-1/2{\cdot}303\boldsymbol{R}T$ as required by the Arrhenius equation, $k = A \exp(-E/\boldsymbol{R}T)$, if A is constant for a series of reactions. It is immediately obvious that for the most part A is not constant, but varies markedly in such a way as to reduce the changes in rate which would otherwise follow the changes in the activation energy. This compensation effect is in some cases so marked that compounds of high activation energy actually decompose faster than those of low activation energy.

(4) If the substituted benzaldehydes are considered as a group related to the unsubstituted compound as a reference standard the following observations can be made:

(*a*) With the exception of an *ortho*-hydroxy-group all *ortho*-substituents reduce the rate slightly, the effect increasing with increasing size of substituent. The rates are, however, not

FIG. 1. *Comparison of substituent effects at* pH 3 *and* pH 5.

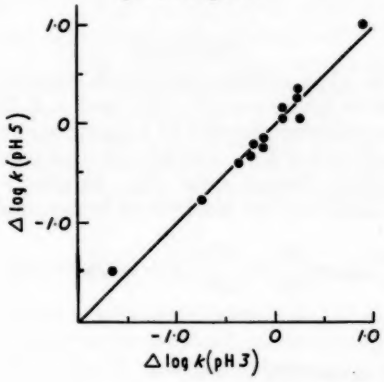


FIG. 2. *Relation between rate and activation energy at* pH 3.

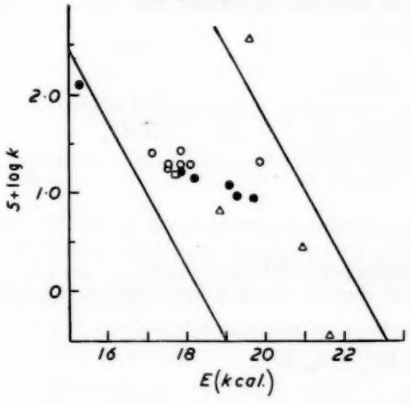
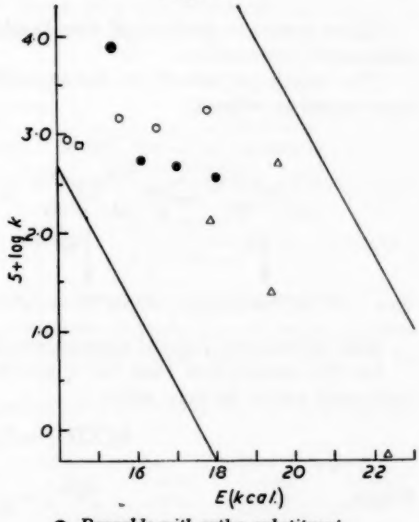


FIG. 3. *Relation between rate and activation energy at* pH 5.



□ *Benzaldehyde.*
○ *Benzaldehyde with* meta- *or* para-*substituent.*
● *Benzalde with* ortho-*substituent.*
△ *Other aldehydehydes and ketones.*

reduced by anything approaching the factor expected on the basis of constant entropy of activation. There is in fact marked " compensation."

(*b*) Without exception *meta*- and *para*-substituents increase the rate slightly despite the fact that most of them raise the activation energy. There is again marked, but less regular compensation.

(*c*) An *ortho*-hydroxy-substituent has a greater effect on the rate than any other substituent in any position. At the upper pH this is due to increased entropy of activation and at the lower pH to reduced energy of activation.

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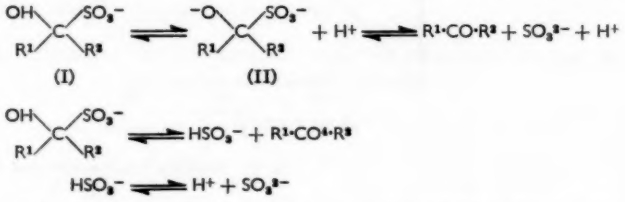
(5) If benzaldehyde itself is chosen to represent the benzaldehyde group the order of increasing rate through the whole series of compounds is as follows: formaldehyde, acetaldehyde, propionaldehyde, *cyclo*hexanone, acetone, benzaldehyde, and chloral. The entropy of activation decreases somewhat in the progression, formaldehyde, acetaldehyde, *cyclo*hexanone, but is markedly reduced in the case of benzaldehyde, and quite appreciably increased in the case of chloral. Acetone seems to occupy an anomalous position.

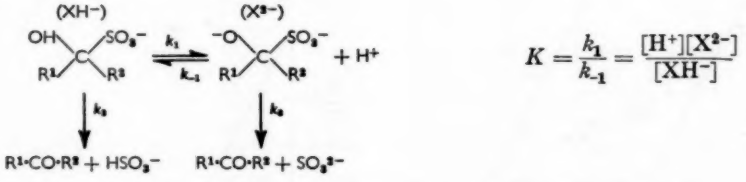
Discussion

(1) *General Mechanism.*—The addition compounds formed by alkali bisulphites and aldehydes or ketones are α-hydroxy-sulphonates and not hydroxy-sulphite esters.[5,6] The addition compound is therefore the salt of a strong acid and is assumed to exist in solution as the singly charged anion (I). This anion is itself a weak acid and will enter into an equilibrium with a doubly charged anion (II). In time, equilibrium would also be established with free bisulphite and free aldehyde or ketone as shown in the scheme:



When iodine is present all free bisulphite is removed from the solution, making its elimination irreversible.

The kinetic picture of the decomposition of an addition compound may therefore be represented as follows:



Rate of reaction (rate of appearance of bisulphite) $= k_2[XH^-] + k_3[X^{2-}]$.

On the assumption that the concentration of doubly charged ions reaches a small stationary value, we may write

$$k_1[XH^-] = k_{-1}[X^{2-}][H^+] + k_3[X^{2-}].$$

Hence

$$[X^{2-}] = \frac{k_1[XH^-]}{k_{-1}[H^+] + k_3}$$

and by substitution we obtain

$$\text{rate} = k_2[XH^-] + \frac{k_1k_3[XH^-]}{k_{-1}[H^+] + k_3}$$

From the experimental data the reaction proved to be of the first order with respect to the addition compound and dependent on the hydroxyl-ion concentration to a power equal to or rather less than unity. The above rate expression gives a satisfactory account

[5] Caughlan and Tartar, *J. Amer. Chem. Soc.*, 1941, **63**, 1265.
[6] Shriner and Land, *J. Org. Chem.*, 1941, **6**, 888.

of these requirements, although for the power to be not much less than unity the first term must make only a small contribution to the observed rate and for most purposes it can probably be neglected.

The simplified rate expression

$$\text{rate} = \frac{k_1 k_3[\text{XH}^-]}{k_{-1}[\text{H}^+] + k_3} \quad (= Kk_3[\text{XH}^-]/[\text{H}^+] \text{ if } k_{-1}[\text{H}^+] \gg k_3)$$

must now be discussed in the light of substituent effects.

(2) *Substituent Effects.*—It is convenient to begin with a consideration of electronic effects in the light of the proposed reaction scheme and Table 2 shows the probable effect of different substituents on the rate constant k_1, k_{-1}, and k_3.

The substituted benzaldehydes form a fairly large group and are discussed first. The effect of *meta*- and *para*-substituents on the rate of reaction is surprisingly small, as shown below. (*ortho*-Substituents do of course exert electronic influences but these are combined with typically " *ortho* "-effects.)

Substituent	*p*-NO_2	*m*-NO_2	*p*-Cl	*p*-Me	*p*-Me_2N	*p*-MeO	*p*-OH
$\Delta \log k$ (pH 3)	+0·06	+0·09	+0·09	+0·09	+0·13	+0·22	+0·24

The results strongly suggest a large-scale cancellation of electronic effects within the molecule and this indeed follows from the proposed reaction scheme where the rate constants are affected in opposite senses (Table 2) by a given substituent and the interplay of changes in these constants will certainly minimise changes in the observed rates. Electron-withdrawing groups have least effect and further ring deactivation would presumably lead to a reduction in the rate since there is no obvious reason why the large-scale annulment of electronic effects should always result in a small net increase in rate for every possible

TABLE 2.

Process	Electron-attracting substituent	Electron-repelling substituent
Ionisation (k_1)	Proton held less firmly. k_1 increased.	Proton held more firmly. k_1 reduced.
Elimination of SO_3^{2-} (k_3)	Negatively charged groups held more firmly. k_3 reduced.	Negatively charged group tends to be forced out. k_3 increased.
Protonation of doubly charged ion (k_{-1})	Proton attracted less strongly. k_{-1} reduced.	Proton attracted more strongly. k_{-1} increased.

substituent or combination of substituents. There is of course the possibility that any substituent, whatever its affinity for electrons, somehow disturbs the solvation pattern round the reactant molecule. This important and probably rather general effect will be discussed in Part II.

With one conspicuous exception *ortho*-substituents tend to reduce the rate in a regular way (Figs. 2 and 3).

Substituent	*o*-OH	*o*-Cl	*o*-NO_2	*o*-MeO	*o*-EtO	*o*-Pr^nO
$\Delta \log k$ (pH 3)	+0·91	+0·01	−0·04	−0·12	−0·21	−0·24
„ (pH 5)	+1·02	—	—	−0·15	−0·22	−0·33

It would appear that the general trend of the results is determined by some special " *ortho* " effect exerted by these substituents rather than by their purely electronic effect. The nature of the effect is discussed later. A characteristic feature is that it is associated with large, regular energy–entropy compensation effects of a rather striking nature, the actual rate of the reaction being in fact little reduced by quite large increases in activation energy.

Thus far the results have been explained in terms of (*a*) a neutralisation of electronic influences and (*b*) a special " *ortho* " effect. All the compounds so far discussed have, however, belonged to the sub-group of substituted benzaldehydes. In their relations with other compounds they may now be represented by benzaldehyde itself.

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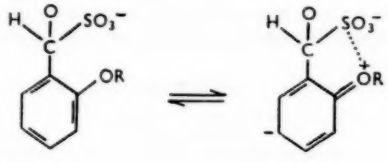
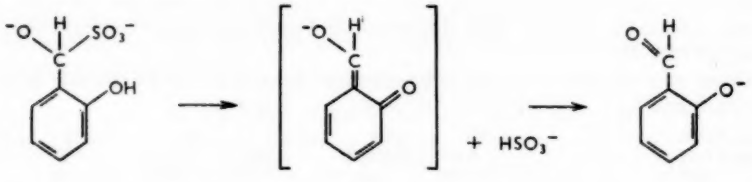
Over the whole series the total spread of rates and activation energies is very much greater than in the sub-group and there is, moreover, over this whole range a less regular compensation effect. Now the mechanism already developed depends on the neutralisation of electronic effects and there is no reason to suppose that this neutralisation ceases to operate outside the benzaldehyde sub-group. It is in fact impossible to attribute the spread in rates to electronic effects because the observed order does not follow variations in the electron affinities of the substituents. There is thus evidence for another kind of steric effect, different from the "*ortho*" effect and causing large changes in activation energy without regular energy–entropy compensation associated with the latter. This new effect is more understandable in the light of information concerning the formation of bisulphite compounds. Benzophenone does not form an addition compound and acetophenone forms one with difficulty and in small amount. If the difficult formation is a manifestation of steric hindrance to the entry of the bisulphite group it may well be matched by a pressure in the compound tending to facilitate the ejection of the bisulphite. The general order and distribution of points on the graph of $\log_{10} k$ against E is therefore understandable in terms of a rather large steric effect depending on the bulk of the groups causing it. Deviations from the general trend are presumably due to special effects, in which the degree of solvation might well be an important factor.

The *ortho*-effect may, under certain conditions, be partly due to the presence of an electrostatic bond. Such a bond would have a retarding influence on the reaction and could be quite strong since an electron-repelling substituent has a full positive charge in three of the four resonance structures



and two equivalent forms.

The apparently anomalous effect of an *ortho*-hydroxy-group is understandable since unlike any other substituent it can be involved chemically in the stages of the reaction. The following is one of several possibilities leading to a large but quantitatively unpredictable increase in the rate of the reaction.



It must be emphasised that the present results manifest once more the tendency for energies and entropies of activation to compensate one another in a series of chemical reactions when certain factors, as yet undefined, come into play. The other substituents in the benzaldehyde sub-group provide a particularly regular case of such compensation. The fact that the measured rate constant is compounded of three separate rate constants in no way reduces the significance of the results. The reason for the compensation effect and its ubiquity will be discussed in Part II (following paper) but at this stage it is important to indicate clearly the specifications to which any data must conform before they can provide real evidence for its existence.

A " correlation " between frequency factor and activation energy may in fact be completely spurious and nothing more than a by-product of errors in the measured activation energies. Warnings [7] have not been completely successful in underlining the hazards of comparing activation energies which come rather close together. The logarithm of the frequency factor has to be calculated from the rate at a given temperature and the activation energy which depends upon measurements over a range of temperatures.

$$\log_{10} A = \log_{10} k + E/2{\cdot}303RT$$

The rate constant is always known to a much higher degree of accuracy than the activation energy and the error in $\log_{10} A$ is therefore directly proportional to the error in the measured activation energy. Suppose a series of reactions gives rise to a series of closely similar experimental rate constants at a given temperature because both energy of activation and frequency factor hardly vary over the series. Experimental errors in the separate activation energies produce, however, corresponding errors in the frequency factors and in fact a very good linear plot of $\log_{10} A$ against E will be obtained. This type of spurious correlation can be easily recognised: a narrow band (of experimental error dimensions) of activation energies coupled with virtually identical rate constants leads to a line of slope $1/2{\cdot}303RT$ on the graph of $\log_{10} A$ against E. With certain assemblies of experimental data the " correlation " slope proves to be the " error " slope. A few " error slopes " are given for purposes of comparison (E in kcal.).

Temperature	0°	10°	20°	40°	60°	100°
" Error slope "	0·80	0·77	0·75	0·70	0·66	0·59

The likelihood of interpreting the results correctly in other cases may now be considered. (i) $\log_{10}$ A *constant*, $\log_{10}$ k *determined by changes in* E. Unless the spread of activation energies is extremely small there is little difficulty in recognising the constancy of the frequency factor. Experimental errors in the activation energy simply scatter the results about the line of constant $\log_{10} A$ on the graph of $\log_{10} A$ against E. (ii) E *constant*, $\log_{10}$ k *determined by changes in* $\log_{10}$ A. If the rate constants are noticeably different then the frequency factors will also differ. Errors in the activation energies will simply scatter the results about the line of constant E on the graph of $\log_{10} A$ against E. (iii) $\log_{10}$ k *determined by simultaneous* (*compensation*) *changes in* E *and* $\log_{10}$ A. The very presence of a compensating effect reduces the spread of the rate constants and great care must be exercised but nevertheless a genuine correlation can be identified provided that (*a*) the activation energies are spread over a sufficiently wide range or (*b*) the rates are spread over a narrower range than the activation energy would indicate.

On the basis of the foregoing observations the data presented in this paper seem to be suitable for inclusion in a general survey of compensation effects. The maximum % error in k is estimated at 5% and is generally a good deal less. Similarly the maximum error in E is about ± 250 cal. Part II (following paper) seeks to fit the results presented in Part I into a more general picture of the extremely varied instances of energy–entropy correlations.

PHYSICAL CHEMISTRY LABORATORY, OXFORD UNIVERSITY. [*Received, February 27th*, 1958.]

[7] Purlee, Taft, and De Fazio, *J. Amer. Chem. Soc.*, 1955, **77**, 837.

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555. *The Kinetics of the Decomposition of the Addition Compounds formed by Sodium Bisulphite and a Series of Aldehydes and Ketones. Part II.* General Discussion of Energy–Entropy Relations.*

By D. A. Blackadder and Sir Cyril Hinshelwood.

In connexion with the experimental study in the preceding paper a general survey, classification, and interpretation of energy–entropy correlations in reaction kinetics is attempted.

Certain of the results given in Part I exhibit a relation between the parameters of the Arrhenius equation. The change in rate over a series of related reactions is lessened by a change in frequency factor tending to offset, in some measure, the effect of a change in activation energy. Effects of this kind are very common but usually left unexplained and their nature is here further discussed in more general terms.

The possibility that certain manifestations of the compensation effect are apparent and not real was discussed in Part I. With the bisulphite addition compounds the compensation associated with the so-called *ortho*-effect is of a regular type indicating the continuous operation of some dominant factor, whereas for other substituents the compensation is characterised by a scatter of experimental points and a less obvious pattern. In general a scatter of results in a kinetic study is attributable either to experimental error or to the interplay of two or more structure-sensitive factors rather nicely balanced with respect to one another. When the same investigation yields results both of marked regularity on the one hand and of considerable scatter on the other, the second explanation for the scatter seems the more likely.

The existence of a rather general compensation effect has long been in evidence.[1] A comprehensive survey of the literature on the subject would be beyond the scope of the present paper but enough examples will be quoted to illustrate the possible types of behaviour. Certain general conclusions can be drawn and the fact emerges that the effect is fundamental and operates according to the same principles in unimolecular or dissociative reactions and in bimolecular or associative reactions.

Much of interest in chemical kinetics comes from the study of related reactions forming a series. It is convenient to consider the simplest molecule capable of undergoing the reaction concerned and to think of modifications of this molecule as causing " substituent effects." These are often resolved into electronic and steric components but the nature of the latter is often obscure. Another convenient parameter variation can be made by considering change of medium. The bond stretching, compressing, and polarisation brought about by substituents in the reacting molecule can equally well be caused by the presence of solvent molecules. In solution there is always an interplay of " substituent " and " solvent " effects whereas in the gas phase substituent effects can be studied in their pure form. Where possible it is convenient to indicate the magnitude of any compensation effect by quoting the slope of the line obtained when log A is plotted against E (in kcal.).

Some Typical Examples.—The decomposition of bisulphite addition compounds described in Part I provides an example of an elimination reaction taking place in solution and there are also some interesting results on the elimination of sulphur dioxide from simple cyclic molecules,[2] the pure molten material being used as solvent medium. At pH 3 and at pH 5, respectively, the results for the bisulphite compounds of *ortho*-substituted benzaldehydes give good lines of slopes 0·61 and 0·64, and indeed the whole of the benzaldehyde sub-group provides evidence for an approximately linear relation between log A and E.

* Part I, preceding paper.

[1] Syrkin, *Z. anorg. Chem.*, 1931, **199**, 28; Schwab, *Z. phys. Chem.*, 1929, *B*, **5**, 406; Evans and Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 1334; Christiansen, *Acta Chem. Scand.*, 1948, **3**, 61; Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

[2] Drake, Stowe, and Partansky, *J. Amer. Chem. Soc.*, 1946, **68**, 2521.

As reported in Part I, however, the complete group of compounds shows an irregular and less marked compensation. The results for the three sulphur dioxide eliminations cover a wide range of activation energies (15 kcal.) and give an excellent line of slope 0·51.

Two interesting unimolecular reactions which have been studied in a series of solvents are the *cis-trans*-isomerisation of azobenzene and of *p*-chlorophenyl diazocyanide.[3] These give slopes of 0·68 and 0·58, respectively, and cover an activation energy range of 5 kcal. The results show some scatter but the variety of solvents used makes the very existence of a compensation effect unusually striking. In the case of *cis*-azobenzene a wide range of solvent media including acetic acid, *cyclo*hexane, and the pure material was covered. Thus " solvent effects " whatever their nature, may sometimes produce correlated shifts in E and log A of very much the same order of magnitude as those produced by structural modifications of a reactant in a constant solvent. In other cases, however, such as the thermal decomposition of *o*-nitrophenyl azide,[4] E and log A are much the same for reaction in a number of solvents and even in the pure liquid medium.

Many bimolecular reactions in solution have been studied but, unlike the unimolecular reactions mentioned above, any given reaction in a series of unrelated solvents usually yields rather irregular results. The benzoylation of *N*-nitroaniline and the reaction between methyl iodide and pyridine,[5] both in a series of solvents, provide examples of highly complex solvent effects.

When modification of a solvent is achieved by varying the relative amounts of two components in a solvent pair rather than by substituting one pure solvent for another definite energy–entropy relations may be observed. The reaction of pyridine and methyl iodide [6] in benzene–ethanol gives a linear plot of log A against E of slope 0·67. This reaction yields quite different results in other solvent pairs such as benzene and nitrobenzene or *iso*propyl ether and nitrobenzene. The energy of activation is here relatively constant over the range of solvent media while log A varies by an amount comparable with that observed in cases where there is correlation and where E varies over a range of about 5 kcal. The scatter of results about a line of constant activation energy is suggestive of the interplay of two effects, and the same type of behaviour is shown by three other reactions involving the formation of quaternary ammonium salts in benzene–nitrobenzene.[7] The alkaline hydrolysis of ethyl benzoate [8] yields a line of slope 0·53, the data including results obtained in pure water and in water–ethanol, water–acetone, or water–dioxan. When water–methanol [9] mixtures are used the same slope is at first found, but at high alcohol content the compensation begins to fail.

The influence of both structure and solvent composition on a bimolecular reaction is well shown by the study of the alkaline hydrolysis of γ-lactones.[10] Two reactions involving rather different ring compounds were studied in water and in three water–ethanol mixtures. The eight experimental points fall on one good line of slope 0·55 and the two sets of four points are in the same order although somewhat displaced relatively to one another. This provides a striking example where both solvent effects and structural effects cause compensations of the same order of magnitude.

Reactions which involve the solvent chemically, not necessarily in the rate-determining stage, form a special group. Tommila and his co-workers have greatly added to data on ester hydrolyses of this type since they have used wide ranges of solvent compositions. They have shown the existence of solvation effects which lead to the appearance of minima when either log A or E is plotted against solvent composition.[11] The results indicate

[3] Hartley, *J.*, 1938, 633; Le Fèvre and Northcott, *J.*, 1949, 944; 1953, 867.
[4] Fagley, Sutter, and Oglukian, *J. Amer. Chem. Soc.*, 1956, **78**, 5567.
[5] Pickles and Hinshelwood, *J.*, 1936, 1353.
[6] Fairclough and Hinshelwood, *J.*, 1937, 1573.
[7] Raine and Hinshelwood, *J.*, 1939, 1382.
[8] Fairclough and Hinshelwood, *J.*, 1937, 541.
[9] Tommila and Ketonen, *Suomen Chem.*, 1945, **18**, *B*, 24.
[10] Hegan and Wolfenden, *J.*, 1939, 508.
[11] Tommila and Hella, *Ann. Acad. Sci. Fenn.*, 1954, *A*, *II*, **53**, 3.

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that even when E varies in a quite complicated manner over a range of solvent compositions the regularity of the compensation may remain unimpaired.

When the solvent is kept constant and a series of related bimolecular reactions is studied even a serious scatter of experimental results may be insufficient to conceal the presence of compensation, as in the reduction of substituted nitrobenzenes by titanous chloride.[12] Some series of solvolytic [13] or replacement [14] reactions show no general energy–entropy correlation even when the data are suitable both in quantity and quality, although there does seem to be a rather general tendency in such cases for the rate changes to follow the changes in activation energy. In many cases, however, the plot of log A against E is regular, and activation energy ranges of up to 10 kcal. are frequently covered. The amine-catalysed decomposition of urethanes in benzyl alcohol [15] is a good example. Substituents in the *meta*- and *para*-positions give points on a line of slope 0·44 and *ortho*-substituents fall on the same line, but in a region of appreciably lower activation energies. The slope for the rearrangement of a series of substituted hydrazobenzenes [16] is 0·64 and a range of 10 kcal. is covered.

Frequently the effects of solvent change and reactant modification are difficultly separable. Energy–entropy correlations of different types may be obtained when stoicheiometrically similar reactions are compared, and evidence for mechanistic dissimilarity may thus be obtained. In aqueous ethanol the base-catalysed hydrolysis of some aromatic amides [17] gives results falling close to a line of slope 0·30 whereas for acid hydrolysis the form of the log A–E relation is a curve concave downwards. Sometimes the results for a series of related solvolytic reactions appear as two or more distinct groups for obvious reasons. In the hydrolysis of some tertiary aliphatic halides,[18] for example, the iodides fall on a good line of slope 0·44 while the chlorides form a group some distance away from it. In other cases, however, it is far from obvious why some of the results should fall on a good line while others lie so far away from it that experimental error offers no explanation. The results for the hydrolysis of the anhydrides of some substituted benzoic acids [19] give a line of slope 0·29 but with a number of points significantly below it. Highly specific solvent effects are presumably operating in these cases. An early paper [20] showed that rather complex behaviour might be expected on varying the structure of an ester in an ester hydrolysis since the nature of the solvent is obviously of great importance, but a good deal of regularity has actually appeared. Sometimes, as in the alkaline hydrolysis of a series of esters of α-hydroxypropionic acid [21] in water or the acid hydrolysis of certain acetates [22] in aqueous acetone, the activation energy ranges are rather narrow, though the slopes of about 0·57 and 0·74, respectively, may be quite genuine. The results for the acid hydrolysis of a series of acetates and benzoates in aqueous ethanol [23] give two lines of slopes 0·76 and 0·51. The same benzoates in aqueous acetone give points very close together and it is interesting to note that in both media the only *ortho*-substituted ester appears to be unlike all the others. In aqueous acetone the alkaline hydrolysis of ethyl esters of substituted benzoic acids, *Bz*-substituted phenyl acetates, or *Bz*-substituted benzyl acetates show a different type of behaviour.[22] For each of the three groups the frequency factor is sensibly constant compared with the changes in activation energy, although as in the case of relatively constant activation energy discussed

[13] Newton, Stubbs, and Hinshelwood, *J.*, 1953, 3384.
[13] Brown, Okamoto, and Ham, *J. Amer. Chem. Soc.*, 1957, **79**, 1906; Brown, Brady, Grayson, and Bonner, *ibid.*, p. 1897.
[14] de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3200.
[15] Mukaiyama and Iwanami, *J. Amer. Chem. Soc.*, 1957, **79**, 73.
[16] Croce and Gettler, *ibid.*, 1953, **75**, 874.
[17] Meloche and Laidler, *ibid.*, 1951, **73**, 1712.
[18] Shorter and Hinshelwood, *J.*, 1949, 2412.
[19] Berliner and Altschul, *J. Amer. Chem. Soc.*, 1952, **74**, 4110.
[20] Newling and Hinshelwood, *J.*, 1936, 1357.
[21] Salmi and Leino, *Suomen Chem.*, 1944, **17**, *B*, 19.
[22] Tommila and Hinshelwood, *J.*, 1938, 1801.
[23] Timm and Hinshelwood, *J.*, 1938, 862.

earlier the results are characterised by a marked scatter. The study of ester hydrolyses has thus further emphasised the general similarity of structural effects and solvent effects with respect to energy–entropy correlations.

Activation Mechanism, Degrees of Freedom, and Ranges of Transition States.—The experimental data for series of reactions in the gas phase are scarce and generally rather imprecise but for reactions in solution they fall into three distinct classes. A relatively rare but important case is that of constant frequency factor. Most common is that associated with marked compensation. The slopes of the log A–E curves do not show a distribution over all possible values but tend to fall in a fairly narrow range. Finally there is the class showing approximately constant activation energy, invariably characterised by a considerable scatter of results, indicative of the interplay of two factors. The simultaneous operation of one factor tending to increase both activation energy and frequency factor, and another tending only to decrease the activation energy, will produce experimental data of the third type.

The operation of such factors can be shown to follow in a very general way from the nature of chemical reactions. Emphasis has sometimes been placed on solvent participation in the transition state [24] but this appears to be only one aspect, though an important one, of a more general phenomenon. Indeed there is a close parallel between phenomena occurring in solution and those in the gas phase. Although suitably documented series of gas reactions are not yet available there are many reactions with apparently abnormally large frequency factors, and this fact itself, as will be shown, is closely connected with the energy–entropy correlation.

In considering variations of rate in a series of reactions the simplest effect to visualise is the electronic influence of a substituent which weakens or strengthens a bond (or bonds) and consequently alters the activation energy. This alteration in E may be progressive and unaccompanied by any change in the entropy of activation.

Solvation may very well modify or even imitate the electronic effect of substituents. Solvent molecules can have a specific action in modifying the influence of individual substituents. If, for example, a substituent of well-marked electrochemical character becomes co-ordinated with a solvent molecule the result may be a considerable modification of its electron-attracting or electron-repelling character, and a corresponding change in reactivity will be manifested by a change in activation energy. This again may be unaccompanied by a change in the entropy of activation. Thus a solvent may exercise an influence in a given reactant molecule kinetically indistinguishable from the classical electronic effect of a substituent. This, however, is far from being the only possible solvent effect, and indeed it would rarely be observed in the absence of other more complex effects. A substituent so far removed from the reaction centre that it is capable of exerting an electronic effect only may yet exert indirect structural effects by a disturbance of the solvent pattern which, as will appear, involves correlated changes in the energy and entropy terms.

In order to see in the most general way how the correlated changes of activation energy and entropy arise it is convenient to start from a well-known fact about unimolecular reactions. Here in the simplest case the entropy term A in the equation $k = A \exp(-E/\boldsymbol{RT})$ is of the order of magnitude of a bond vibration frequency, the condition for this being that the activation energy is concentrated in one bond in the transition state. That is, there is one critical vibrational degree of freedom in the transition state. But the term A often assumes a value several powers of ten greater than the vibration frequency, the interpretation being that the activation energy is not strictly localised but can be distributed in any way between S degrees of freedom. In these conditions the probability of a transition state is increased by a combinatory factor in which the major term is $(E/\boldsymbol{RT})^{S-1}/(S-1)!$. There is now a whole range of equivalent transition states and the entropy of activation is increased. If there are many states

[24] Wynne-Jones and Eyring, *J. Chem. Phys.*, 1935, **3**, 492.

of equivalent energy there must lie, somewhere between them in the appropriate configuration space, a minimum of lower energy. This minimum will presumably correspond to reaction through one transition state only, that in which the activation energy is concentrated in one bond. In a series of reactions there may be varying displacements from the path of minimum activation energy and this circumstance will therefore result, by the operation of the combinatory factor, in corresponding changes in the entropy of activation. This seems to be the essence of an energy–entropy correlation in so far as it may occur in a unimolecular gas-phase reaction.

At first sight the problem of bimolecular reactions appears to be different. Closer consideration, however, shows it to be governed by basically similar principles. According to a commonly applied theorem the energy of activation in a three-centre reaction $A + BC \longrightarrow AB + C$ is a minimum when the transition state is linear, that is when A approaches along the axis of BC which may be taken as the x-axis. A must possess a component of velocity u_x in this direction corresponding to a kinetic energy E' which constitutes part of the activation energy E. Consider next the possibility of an oblique approach along an axis making an angle α with the x-axis. The component in the direction x will not be less than u_x and there must now be an additional component at right angles to x of not less than $u_x \tan \alpha$, say r. It does not matter what the components of r in the directions y and z are so long as $u_y^2 + u_z^2 = r^2$. Thus some at least of the additional activation energy is not contained in one degree of freedom but distributed in any proportion between two degrees of freedom. If an amount E'' is involved then the probability of its presence is not $\exp(-E''/RT)$ but $(E''/RT)\exp(-E''/RT)$. If then the reaction forsakes the path of minimum activation energy, then from the very nature of a minimum, displacement towards a whole range of states of equal energy occurs, all of which are equally likely to lead to reaction. The result is an increase in the entropy factor which works against the effect of the increased activation energy. At first sight the most obvious circumstance imposing the oblique reaction path would be blocking of the path of minimum energy by a steric effect. There is, however, a more general possibility. The measured activation energy represents the most frequently followed reaction path. This may not be that of minimum energy, if for some other set of paths, removed from it, the product of the exponential energy factor and of the entropy factor is greater. The entropy increase appears in the appropriate form of rate equation as a combinatory factor representing the increased probability of a given total energy when shared between multiple degrees of freedom. Much more complex conditions than those schematised in the three-centre problem occur in many bimolecular reactions. The absolute minimum activation energy may be a minimum in a space of many dimensions. Displacements from it can occur in many ways and it is surrounded by a very complex range of states of equal higher energy. This range is in turn surrounded by another more extensive range of states of even higher energy. In a series of reactions structural changes will alter the shape of the energy surfaces, and the reaction path followed will be the accessible one giving the greatest product of the exponential term and the combinatory factor. Rises in the activation energy due to departure from the minimum will then generally be compensated to some extent.

The participation of a solvent may lead to a further multiplication of the number of equivalent transition states. Reactants and products are often unequally solvated and the activated complex may be more or less solvated than the reactant: the result will be a correlated change in the energy and entropy factors. As exemplified in a discussion by Tommila,[11] if the activated complex is more heavily solvated than the reactant, then the spontaneous process of solvation, tending to reduce the potential energy, will cause a lowering of the activation energy. This type of solvent participation must, however, lower the entropy of activation since more molecules are now involved in the definition of the transition state. If, on the other hand, the attainment of the transition state involves a release of solvent molecules initially bound to the reactant, energy must be

supplied for the purpose and E will be increased. The provision of energy for the break up of a more or less elaborate solvent pattern may, however, be achieved in many different ways and there is likely to be considerable latitude in the manner in which this energy is shared between what are virtually new degrees of freedom. The above-mentioned combinatory factor thus enters into the expression for the energy distribution and the pre-exponential factor of the Arrhenius equation therefore increases, because the new transition states, although of higher energy, are more numerous.

Classification of Energy–Entropy Correlations

The various kinds of energy–entropy relations may now be conveniently classified. Both "substituent effects" and "solvent effects" fall naturally into line with one another under the different headings, and indeed cannot be separated from one another when both operate together.

I. *Substituent Effects.*—(i) Bond strengths are altered but the form of the transition state is unchanged since the number of degrees of freedom involved in the activation process remains the same. This corresponds to the classical electronic effect and only the activation energy is altered.

(ii) For steric reasons the structural change modifies the contour lines surrounding the activation energy minimum. The number of degrees of freedom involved is increased and thus there is a correlated increase in the energy and entropy terms.

(iii) The structural change imposes a new solvation pattern on the system so that the modified reactant is virtually in a modified solvent. Correlated changes in the energy and entropy terms may appear.

II. *Solvent Effects.*—(i) The solvation pattern changes when the solvent is varied and correlated changes in the energy and entropy terms are caused.

(ii) The specificity of solvent–solute interactions is such that changes from one solvent to another may produce effects equivalent to those produced by changing a substituent in the reactant, an individual substituent group being itself more or less profoundly modified by the solvent. Any of the energy–entropy relations may result here.

In addition to the general classificaton given above there are of course energy–entropy variations due to changes in frequency, mass, and moment of inertia terms which appear in the partition functions describing the transition state. The influence of these effects, however, will be largely outweighed when for one or more of the reasons discussed above there is a significant modification of the relation between activation energy and the number of equivalent transition states. A more detailed knowledge of the operation of the large-scale effects is the primary requirement at present.

Dissociation of Bisulphite Compounds

The broad general classification of energy–entropy relations covers all the cases discussed. In particular, it allows for the operation of both aspects of the correlation postulated in Part I. In the first place substitution of formaldehyde causes a decrease in activation energy with a moderate and irregular compensating decrease in the entropy of activation. In the second place substitution of benzaldehyde brings about similar energy and entropy changes which are rather irregular but nevertheless marked, except in the case of *ortho*-substituents where the compensation is both marked and regular. The increase in activation energy caused by *ortho*-substituents is more or less proportional to the size of the group concerned, in contrast to the effect of substitution on formaldehyde.

In the first case the effect is steric in the sense that it is unrelated to the polarity of the substituent. If the group R or R′ is bulky, entry of the bisulphite group into the ketone R·CO·R′ will be more difficult than into formaldehyde, and the strain in the compound correspondingly greater, with the result that there will be a pressure tending to expel the

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group and so lower the activation energy of the decomposition. The chief consequence will therefore be the change in E. The irregular entropy compensation seems here most likely to be due to varying combinations of the factors which have been discussed, the influence of the activation energy on the whole remaining dominant.

In the second case the substituents in the benzene ring presumably disrupt the solvent pattern besides exerting electronic effects with consequences which have already been considered. The *ortho*-substituted molecules represent a rather special sub-group, for the progressive stabilisation of the addition compound by increasingly bulky groups would seem to demand an explanation in terms of an interaction between the substituent and the bisulphite group itself. This could hardly occur without a considerable effect on the solvation pattern in the neighbourhood of the reaction centre, and a strong energy–entropy correlation could thus be caused.

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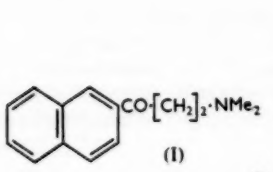
556 *Polycyclic Systems. Part II.* Synthesis of Some Chrysene and Hydrochrysene Derivatives.*

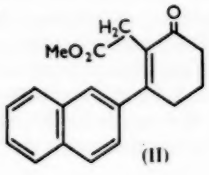
By D. NASIPURI, A. C. CHAUDHURI, and J. ROY.

The methiodide of 2-dimethylaminoethyl β-naphthyl ketone (I) on usual Mannich-base condensation with methyl β-oxoadipate gives methyl 2-β-naphthyl-6-oxo*cyclo*hex-1-enylacetate (II). The latter provides a simple route to chrysene and hydrochrysene derivatives and has been employed for the synthesis of octahydro-1-oxo- and -1 : 11-dioxo-chrysenes. A preliminary account of this work has already appeared.[1]

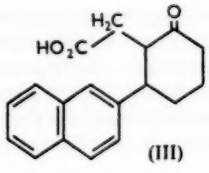
2-DIMETHYLAMINOETHYL β-NAPHTHYL KETONE (I), prepared by Blicke and Maxwell's method,[2] gave a crystalline methiodide which reacted with the potassium derivative of methyl β-oxoadipate. The product, on hydrolysis and re-esterification, afforded methyl 2-β-naphthyl-6-oxo*cyclo*hex-1-enylacetate (II) in about 30% overall yield. The ester on



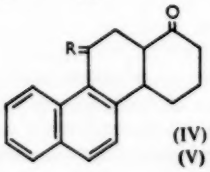
(I)



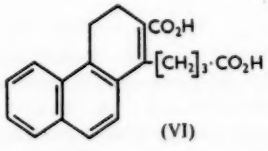
(II)



(III)



(IV) : R = O
(V) : R = H_2



(VI)

hydrogenation in presence of colloidal palladium and subsequent saponification gave the acid (III) which was isolated mainly in one stereoisomeric form. The latter was cyclised with polyphosphoric acid to 1 : 2 : 3 : 4 : 4*a* : 11 : 12 : 12*a*-octahydro-1 : 11-dioxochrysene (IV) in good yield, which was hydrogenated by the use of platinum–palladium[3] to the

* Part I, Nasipuri, *J.*, 1958, 2618.

[1] Nasipuri, Chaudhuri, and Roy, *Chem. and Ind.*, 1957, 422.
[2] Blicke and Maxwell, *J. Amer. Chem. Soc.*, 1942, **64**, 428.
[3] (*a*) Zelinsky, *Ber.*, 1933, **66**, 872; (*b*) Koebner and Robinson, *J.*, 1938, 1994.

octahydro-1-oxochrysene (V). This stage was analogous to the synthesis of the corresponding hydro*cyclo*pentenophenanthrene derivatives by Robinson and his co-workers;[4] but while, in the latter case, the products were presumably the *cis*-isomers,[5] these hydrochrysene ketones were expected to be more stable in *trans*-configuration. In fact, the ketone (V) on treatment with mineral acid was recovered mostly unchanged. An authentic specimen of this ketone was prepared by an alternative route from γ-(2-carboxy-3 : 4-dihydro-1-phenanthryl)butyric acid (VI) (cf. Part I). The latter was reduced by sodium amalgam, and the derived diethyl ester on Dieckmann cyclisation and subsequent hydrolysis afforded the ketone (V).

The diketone (IV) was converted into chrysene by reduction with lithium aluminium hydride, followed by aromatisation with 10% palladium–charcoal.[6] The ketone (V) was converted into 1-methylchrysene by the standard procedure.

Experimental

Methyl 2-β-*Naphthyl*-6-*oxo*cyclo*hex*-1-*enylacetate* (II).—A mixture of methyl β-naphthyl ketone (17 g.), dimethylamine hydrochloride (8·3 g.), paraformaldehyde (4·5 g.), absolute ethanol (30 ml.) and concentrated hydrochloric acid (0·5 ml.) was refluxed on the steam-bath for 3 hr. Most of ethanol was removed at the water-pump, and the crystalline hydrochloride was dissolved in the minimum quantity of water and basified with an excess of 40% potassium hydroxide solution. The amino-ketone was extracted with ether, dried (K_2CO_3), and evaporated. The residue (21 g.) was taken up in dry benzene (75 ml.) and cooled in ice, methyl iodide (7 ml.) was added dropwise during 30 min. with stirring, and the whole was left overnight at 0°. Next day, to the cold mixture was added a solution of methyl β-oxoadipate (19 g.) in benzene (25 ml.), followed by ethanolic potassium ethoxide [from potassium (6 g.) in ethanol (100 ml.)]. Air in the flask was displaced by nitrogen and the mixture was stirred in the cold for 1 hr., then refluxed for 30 min. The cooled solution was decomposed with 2N-sulphuric acid, and the benzene layer was separated. The aqueous solution was extracted with ether, and the combined organic layers were washed with water and dried. On their evaporation a gum (36 g.) was left which was hydrolysed by potassium hydroxide (30 g.) in boiling water (900 ml.) for 6 hr. under nitrogen. The alkaline solution was once extracted with ether, then cautiously acidified. The precipitated acid (20 g.) was taken up in ether and esterified by refluxing methanolic 2·5% hydrochloric acid (150 ml.). The *methyl ester* boiled at 220—230°/0·1 mm. and on crystallisation from methanol afforded prisms (9·3 g., 31%), m. p. 131° (Found: C, 77·5; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·6; H, 6·1%), $\lambda_{max.}$ 219, 265, and 287 mμ (log ε 4·73, 4·33, and 4·04). The *acid* obtained on hydrolysis crystallised from aqueous acetone in needles, m. p. 156° (Found: C, 77·1; H, 5·8. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·7%) and gave a *semicarbazone*, m. p. 218° (Found: C, 67·3; H, 5·7; N, 12·9. $C_{19}H_{19}O_3N_3$ requires C, 67·7; H, 5·7; N, 12·5%).

2-β-*Naphthyl*-6-*oxo*cyclo*hexylacetic Acid* (III).—The foregoing ester (II) (10·5 g.) was shaken in ethanol (200 ml.) with hydrogen, palladium chloride (0·2 g.), and gum arabic (0·2 g.) at 40°. Absorption of hydrogen (1050 ml., 1 mol.) was complete in 4 hr. The solution was filtered and hydrolysed by refluxing aqueous 10% potassium hydroxide (40 ml.). The *acid*, on crystallisation from acetic acid, melted at 143—148°. After several crystallisations from aqueous acetone, the m. p. rose to 170—172° (Found: C, 76·5; H, 6·4. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). The *semicarbazone* formed prisms (from ethanol), m. p. 228° (Found: C, 67·1; H, 6·3; N, 12·6. $C_{19}H_{21}O_3N_3$ requires C, 67·3; H, 6·2; N, 12·4%).

1 : 2 : 3 : 4 : 4*a* : 11 : 12 : 12*a*-*Octahydro*-1 : 11-*dioxochrysene* (IV).—The acid (III) (3 g.) was kept in with polyphosphoric acid [from phosphoric oxide (10 g.) and 89% phosphoric acid (8 ml.)] at 70—75° for 2 hr., then decomposed with ice and extracted with benzene. The extract was washed with dilute sodium hydroxide solution, then with water. The *diketone* obtained on evaporation crystallised from methanol in needles (2·4 g., 80%), m. p. 158—160°, increased by several crystallisations to 175° (Found: C, 82·0; H, 6·2. $C_{18}H_{14}O_2$ requires C, 81·8; H, 6·1%). It had $\lambda_{max.}$ 214, 247, and 318 mμ (log ε 4·91, 4·70, and 4·25). The *semicarbazone* formed a powder (from acetic acid), m. p. 264—266° (decomp.) (Found: C, 70·8; H,

[4] Robinson, *J.*, 1938, 1390; also ref. 3*b*.
[5] Birch, Jaeger, and Robinson, *J.*, 1945, 582.
[6] Linstead and Thomas, *J.*, 1940, 1127.

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6·1; N, 13·3. $C_{19}H_{19}O_2N_3$ requires C, 71·0; H, 5·9; N, 13·1%). The red dinitrophenylhydrazone had m. p. 274—275° (decomp.).

Chrysene.—The above diketone (0·5 g.) was reduced by lithium aluminium hydride (0·5 g.), and the crude diol (0·52 g.) was heated with 10% palladium–charcoal (0·1 g.) at 280° for 2 hr. The melt was taken up in hot benzene and filtered. The filtrate, on cooling, afforded chrysene in plates (0·36 g., 80%), m. p. 243—246°. On further crystallisation from toluene, it melted at 250° alone or mixed with an authentic sample (Found: C, 94·5; H, 5·3. Calc. for $C_{18}H_{12}$: C, 94·7; H, 5·3%). The trinitrofluorenone complex formed yellow needles (from ethanol), m. p. and mixed m. p. 248—249° (Found: N, 7·9. Calc. for $C_{18}H_{12},C_{13}H_5O_7N_3$: N, 7·7%); Orchin and Woolfolk [7] given m. p. 247·8—249°.

1 : 2 : 3 : 4 : 4*a* : 11 : 12 : 12*a*-*Octahydro*-1-*oxochrysene* (V).—(*a*) The diketone (IV) (1 g.) was reduced in ethanol (30 ml.) by hydrogen in presence of palladium–platinum–charcoal as described by Koebner and Robinson.[3b] The *ketone* (V) crystallised from benzene–light petroleum (b. p. 40—60°) in prisms, m. p. 161—162° (Found: C, 86·4; H, 7·4. $C_{18}H_{18}O$ requires C, 86·4; H, 7·2%). The *dinitrophenylhydrazone* formed a yellow powder, m. p. 265—266° (decomp.) (Found: N, 13·1. $C_{24}H_{22}O_4N_4$ requires N, 13·0%).

(*b*) γ-(2-Carboxy-3 : 4-dihydro-1-phenanthryl)butyric acid (5 g.) was reduced in 2% aqueous potassium hydroxide (100 ml.) by gradual addition of 2·5% sodium amalgam (200 g.). The solution was filtered and acidified. The gummy acid was worked up in the usual way and with ethanolic sulphuric acid gave an ester, b. p. 220—230°/0·1 mm. The ester (3 g.) was heated with finely powdered sodium (0·21 g.) and dry benzene (12 ml.) on the steam-bath for 2 hr. The resultant β-oxo-ester was hydrolysed by refluxing hydrochloric acid (10 ml.) and acetic acid (20 ml.) for 5 hr. The ketone (V) was worked up in the usual way and crystallised from benzene–light petroleum in prisms, m. p. and mixed m. p. 163—164° (Found: C, 86·4; H, 7·4%). The dinitrophenylhydrazone formed a yellow powder (from acetic acid), m. p. 266—268° (decomp.). The ketone gave readily a *furfurylidene derivative* which crystallised from ethyl acetate in light yellow needles, m. p. 178—179° (Found: C, 84·0; H, 6·2. $C_{23}H_{20}O_2$ requires C, 84·1; H, 6·1%).

1-*Methylchrysene.*—A solution of the foregoing ketone (V) (0·2 g.) in benzene (15 ml.) was treated with excess of methylmagnesium iodide, and the product (0·2 g.) was heated with 10% palladium–charcoal at 280° for 2 hr. The melt was extracted with benzene, and 1-methylchrysene obtained from the extract crystallised from toluene, forming leaflets, m. p. 249° (Found: C, 94·1; H, 5·7. Calc. for $C_{19}H_{14}$: C, 94·2; H, 5·8%). Bachmann and Struve [8] give m. p. 249·5—250°.

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[7] Orchin and Woolfolk, *J. Amer. Chem. Soc.*, 1946, **68**, 1727.
[8] Bachmann and Struve, *J. Org. Chem.*, 1940, **5**, 416.

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557. *Production of Mannitol by a* Lactobacillus *causing Ropiness in Cider.*

By S. A. BARKER, E. J. BOURNE, ELISABETH SALT, and M. STACEY.

The major change in carbohydrate content effected during growth of a ropy-cider organism on a medium containing apple juice and yeast extract is production of mannitol from the fructose present in the apple juice. The nature of the " ropy " precipitate is discussed.

ROPY cider is cider which has become highly viscous and when poured from a bottle forms a wide continuous stream. This disorder is generally accompanied by turbidity and deposition of a " ropy " precipitate. One of the most common producers of ropiness in cider was isolated by Millis [1] and shown to be a Gram-positive *Lactobacillus* which was

[1] Millis, Ph.D. Thesis, Bristol, 1951.

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related to, but not identical with, *L. brevis*, *L. buchneri*, and *L. pastorianus*. The object of the present investigation was to determine the changes brought about by this *Lactobacillus* in a medium containing apple juice and yeast extract, with particular reference to the carbohydrate constituents.

Fractionation of sugars, oligosaccharides, and smaller molecules present in ropy apple juice was effected on a charcoal column.[2] The major component isolated from the aqueous eluate was crystalline mannitol which was characterised by its infrared spectrum and its rotation in borate solution and as its hexa-acetate. The glucose and fructose detected in the mother-liquors were characterised as their *O-iso*propylidene derivatives. Galacturonic acid and amino-acids were also found in the aqueous eluate. From the fractions eluted with aqueous ethanol crystalline sucrose and two trisaccharides were obtained. Examination of the sugars present in the original medium indicated that the major change effected by the ropy-cider organism was the production of mannitol. Quantitative determination of the changes occurring (Table 1) confirmed this and showed the gradual disappearance of glucose, fructose, and amino-acids.

TABLE 1. *Changes effected by the ropy-cider organism.*

Time of growth (days)	pH	% w/v pptd. by 2 vols. of EtOH	Mannitol (%) isolated (corr.)	Total reducing substances (%)	Fructose (%)	Glucose (%)	Amino-acids (%) (corr.)
0	4·96	0·28	—	7·57	5·0	2·57	0·717
1	4·75	0·31	—	6·85	—	—	—
2	—	0·27	0·74	6·90	4·79	2·11	—
3	4·30	0·26	2·14	4·85	3·70	1·15	0·757
4	—	0·28	2·84	3·24	—	—	0·600
6	—	0·29	3·76	2·82	—	—	—
8	—	0·25	3·92	1·78	1·50	0·28	0·432
9	—	0·32	4·57	1·39	1·15	0·24	—
11	4·08	0·23	5·00	—	—	—	—
16	4·25	0·28	4·51	0·84	—	—	—
20	—	0·25	4·96	0·79	0·72	0·07	0·614
32	4·00	0·27	4·87	0·19	—	—	0·311

The soluble polysaccharide fraction ($[\alpha]_D$ +48·8°) in ropy apple juice was isolated by dialysis, fractionation with " Cetavlon " (cetyltrimethylammonium bromide),[3] to remove nucleic acid, and removal of proteins by Sevag, Lackman, and Smolens's method.[4] On hydrolysis it gave mannose, glucose, galactose, and arabinose. This polysaccharide fraction was separated into a mannan, $[\alpha]_D$ +75·6° (isolated *via* its copper complex), and a polysaccharide, $[\alpha]_D$ +18·0°, incorporating glucose, galactose, and arabinose. A mannan with $[\alpha]_D$ +76·2° was present in the original yeast extract. A polysaccharide fraction isolated from the original apple juice and also incorporating glucose, galactose, and arabinose showed a higher specific rotation (+60·0°) than that present in ropy apple juice. The amount of material which was isolated by addition of 2 volumes of ethanol to cultures of ropy cider grown for various times (Table 1) and would contain the soluble polysaccharides remained almost constant.

Analysis of the ropy precipitate after extraction with sodium cholate [5] indicated that it consisted of protein, tannin (cf. Williams [6]), nucleic acid, and a polysaccharide fraction containing mannose and glucose units.

The ropy-cider organism was grown on synthetic media containing glucose or fructose, ascorbic acid, and yeast extract in mineral medium. The results suggested that, while glucose speeds the initial growth of the organism, fructose is needed for the formation of both the characteristic ropy mucilage and mannitol.

[2] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[3] Dutta, Jones, and Stacey, *Biochim. Biophys. Acta*, 1953, **10**, 607, 613.
[4] Sevag, Lackman, and Smolens, *J. Biol. Chem.*, 1938, **124**, 425.
[5] Henry and Stacey, *Nature*, 1943, **151**, 671.
[6] Williams, Ann. Rept. Agr. Hort. Res. Sta. Long Ashton, Bristol, 1952, p. 219.

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Experimental

Preparation of Ropy Apple Juice.—Depectinised Bramley's Seedling apple juice containing 1% of "Difco" yeast extract was passed through a Seitz filter, adjusted to pH 4·8, and sterilised in an autoclave for 15 min. at 7—10 lb. per sq. in. The sterile medium was inoculated with the ropy-cider organism and incubated for 11—14 days at 30°/4 cm. in a vacuum-desiccator over 25% aqueous sodium hydroxide and pyrogallol.

Fractionation of Ropy Apple Juice.—(a) *Sugars.* The ropy medium (400 c.c.) was centrifuged, neutralised, and fractionated [2] on a charcoal column (21 × 3·8 cm.). Paper chromatography and ionophoresis [7] of the aqueous eluate (1600 c.c.) showed the presence of, *inter alia*, glucose, fructose, galacturonic acid, and amino-acids. The freeze-dried eluate (51·15 g.) gave mannitol (14·05 g.), m. p. and mixed m. p. 164—166·5°, $[\alpha]_D^{17}$ +28·7° (*c* 0·627 in aqueous borate) (confirmed by infrared analysis) (Found: C, 40·0; H, 8·0. Calc. for $C_6H_{14}O_6$: C, 39·5; H, 7·75%). Acetic anhydride and zinc chloride gave mannitol hexa-acetate, m. p. and mixed m. p. 123·5—125° (Found: C, 49·6; H, 6·0. Calc. for $C_{18}H_{26}O_{12}$: C, 49·7; H, 5·9%). A portion (5·29 g.) of the residual elute, absorbed on kieselguhr (10 g.), was shaken with acetone (98·8 c.c.) and concentrated sulphuric acid (5·2 c.c.) for 6 hr. Partial hydrolysis (Bell [8]) gave a product (1·07 g.), m. p. 91·5—93·5° undepressed on admixture with 2 : 3-4 : 5-di-*O*-*iso*propylidene D-fructopyranose and showing $[\alpha]_D^{18\cdot5}$ −24·9° (*c* 0·802 in $CHCl_3$) (Found: C, 55·7; H, 7·6. Calc. for $C_{12}H_{20}O_6$: C, 55·35; H, 7·75%). A second product (0·07 g.) had m. p. 150—152° undepressed on admixutre with 1 : 2-*O*-*iso*propylidene-D-glucose (Found: C, 48·55; H, 7·1. Calc. for $C_9H_{16}O_6$: C, 49·1; H, 7·3%).

Further elution with aqueous ethanol (2·5%, 500 c.c.; and 5%, 2·2 l.) gave a fraction (2·418 g.) containing amino-acids and a component identical in its paper chromatographic behaviour with sucrose. The latter crystallised from methanol and had m. p. and mixed m. p. 168—170°, $[\alpha]_D^{17}$ +65·6° (*c* 0·87 in H_2O) (Found: C, 42·1; H, 6·45. Calc. for $C_{12}H_{22}O_{11}$: C, 42·1; H, 6·5%).

Elution with 9 : 1 water–ethanol (1·7 l.) gave a fraction (0·371 g., $[\alpha]_D^{17}$ +28·8° in H_2O) which contained a single component with the mobility of a trisaccharide.[9] Acid hydrolysis gave glucose and fructose (identified paper-chromatographically). Another fraction (0·239 g.) eluted with 85 : 15% water–ethanol (1 l.) had $[\alpha]_D^{17}$ +11·8° in H_2O and contained two similar trisaccharides.

(b) *Polysaccharides.* Ropy apple juice (2640 c.c.) was dialysed against running water for 7 days. The insoluble material (2·224 g.) was removed by centrifugation and the soluble material (5·372 g.) recovered by concentration and freeze-drying. The latter material was redissolved in water and "Cetavlon" (cetyltrimethylammonium bromide) added until there was no further precipitation. The supernatant solution was then submitted to 22 Sevag separations [4] which removed most of the protein. The polysaccharide fraction (2·360 g.) remaining in solution had $[\alpha]_D^{17}$ +48·8° (*c* 0·431 in H_2O). Paper-chromatographic examination of its hydrolysate (2N-sulphuric acid at 100° for 4 hr.) showed the presence of mannose, glucose, galactose, and arabinose. Part (0·595 g.) of this polysaccharide was refractionated. On addition of alkaline Fehling's solution some of the polysaccharide (0·161 g.) was precipitated as a copper complex. The free polysaccharide had $[\alpha]_D^{18}$ +75·6° (*c* 0·40 in H_2O) and examination of its hydrolysate (as above) showed that it contained only mannose with a trace of galactose. The polysaccharide (0·035 g.) recovered from the supernatant solution had $[\alpha]_D^{18}$ +18·0° (*c* 0·54 in H_2O) and chromatography of its hydrolysate indicated the presence of glucose, galactose, and arabinose with a trace of mannose.

(c) *Insoluble ropy material.* The insoluble material, collected from ropy apple juice (900 c.c.) which had been incubated for 7 days, was thoroughly washed with water and then suspended in 2% aqueous sodium cholate [5] (38 c.c.). This suspension was added dropwise during 1 hr. to a further quantity of 2% aqueous sodium cholate (50 c.c.) at 60°. After cooling, the insoluble fraction A (0·444 g.) was recovered and the supernatant solution dialysed to remove sodium cholate. Further insoluble material B (0·323 g.) which separated was collected at the centrifuge. Addition of "Cetavlon" to the supernatant liquid gave fraction C (0·104 g.). A further fraction D (0·015 g.) was recovered by addition of two volumes of ethanol.

[7] Foster, *J.*, 1953, 982.
[8] Bell, *J.*, 1947, 1461.
[9] Barker and Carrington, *J.*, 1953, 3588.

Fractions A, B, C, and D were each hydrolysed (as above) and the hydrolysates analysed by paper chromatography and ionophoresis. Glycerol was found in A before hydrolysis. The hydrolysate of A contained glucose, glycerol, at least five amino-acids (one of which was arginine), and several unidentified components one of which could be detected by fluorescence in ultraviolet light and developed a yellow colour with ammonia: this component was believed to be chlorogenic acid. Fraction B contained no glycerol and after hydrolysis produced glucose, at least six amino-acids, and a component believed to be chlorogenic acid. The hydrolysate of fraction C contained ribose, glucose, glycerol, and amino-acids. The major component of fraction C was nucleic acid since it showed an ultraviolet absorption peak at 258 mμ, contained phosphorus, and on alkaline hydrolysis [10] gave cytidylic, adenylic, guanylic, and uridylic acid. Fraction D showed no ultraviolet absorption and the hydrolysate contained mannose and glucose.

Examination of Original Apple Juice.—Examination of depectinised Bramley's Seedling apple juice by paper chromatography and ionophoresis showed the presence of glucose, fructose, and small amounts of aspartic acid, glutamic acid, and neutral amino-acids.

Apple juice (500 c.c.) was dialysed against running water for six days; the soluble polysaccharide (0·311 g.), isolated as above, had $[\alpha]_D^{18}$ +60·0° (*c* 0·20 in H_2O). Analysis of the hydrolysate showed the presence of glucose, galactose, and arabinose.

Examination of Difco Yeast Extract.—No reducing sugars were detected in the yeast extract but spraying paper chromatograms with silver nitrate [11] disclosed a component with an R_F value similar to that of trehalose. Large amounts of amino-acids including aspartic acid, glutamic acid, arginine, and lysine were detected in the yeast extract.

1% Difco yeast extract (490 c.c.), treated as above, gave a soluble polysaccharide fraction (1·48 g.), $[\alpha]_D^{18}$ +27·8° (*c*, 0·54 in H_2O), which gave mannose together with a trace of glucose on acid hydrolysis. Formation of the copper complex and purification involving extraction with trichloroacetic acid [12] gave a mannan, $[\alpha]_D^{18\cdot5}$ +76·2° (*c* 1·3 in H_2O).

Quantitative Determination of the Changes occurring in Ropy Apple Juice.—Thirty-eight graduated tubes each containing the standard apple juice–yeast extract medium (20 c.c.) were sterilised and inoculated. At intervals after incubation at 30° some of the cultures were centrifuged and filtered through a No. 4 sintered-glass filter. The pH of each solution was measured and then a known volume mixed with two volumes of ethanol to precipitate any soluble polysaccharide. In selected cases, the aqueous-alcoholic solutions remaining after precipitation of the polysaccharide were concentrated to a small volume to remove alcohol and then passed down a column (30 × 1 cm.) of Amberlite IRA-400 (OH^-). The mannitol was eluted with carbon dioxide-free water (300 c.c.; flow rate 5 c.c./min.), and the eluate neutralised, concentrated to a syrup, and extracted with methanol. Mannitol crystallised from the methanol extract when present and the eluate had zero optical rotation in all cases. When the mannitol was recovered from two solutions of mannitol (3·88%), fructose (6·69%), glucose (2·41%), sucrose (0·70%), and tannic acid (0·79%) by this standard procedure the recoveries were 87·0% and 90·7% respectively. The total reducing substances in the concentrated aqueous alcoholic solutions remaining after precipitation of the polysaccharide were determined by the Shaffer–Hartmann method.[13] Fructose was determined by the van der Plank method,[9] and the difference between the value for total reducing sugars and fructose was assumed to be due to glucose. For the determination of amino-acids the solution was passed down a column of Zeo-Karb 215 (H^+) which was washed with water until zero optical rotation indicated the complete removal of sugars. The column was then eluted with 3N-ammonia until the effluent gave no test for amino-acids with ninhydrin.

A standard solution (10 c.c.) containing arginine (0·073 g.), glycine (0·080 g.), glutamic acid (0·074 g.), fructose (0·261 g.), glucose (0·178 g.), and mannitol (0·254 g.) was separated in this way and gave an 87% recovery of amino-acids (0·197 g.). The results of the experiments are given in Table 1.

Growth of Ropy-cider Organism in Synthetic Media.—A medium was prepared containing fructose (9·06%), ascorbic acid (0·29%), Difco yeast extract (0·92%), magnesium sulphate (0·2%), sodium nitrate (0·2%), and ammonium sulphate (0·2%). A similar medium in which

[10] Davidson and Smellie, *J.*, 1952, 594.
[11] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[12] Hiller and van Slyke, *J. Biol. Chem.*, 1922, **53**, 253.
[13] Shaffer and Hartmann, *ibid.*, 1921, **45**, 365.

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glucose (9·11%) replaced the fructose was also prepared and after sterilisation both were inoculated with the ropy-cider organism and incubated (as above). Growth in fructose medium was slow and of a characteristic ropy nature, whereas in the glucose medium growth was fast and the precipitate powdery. The results of analyses are given in Table 2. Hydrolysis

TABLE 2. *Growth in synthetic media.*

Inoculation (days)	pH	Mannitol (%) (corr.)	Total reducing substances (%)	% (w/v) pptd. with 2 vols. of EtOH	Inoculation (days)	pH	Mannitol (%) (corr.)	Total reducing substances (%)	% (w/v pptd. with 2 vols. of EtOH
Glucose medium					*Fructose medium*				
0	4·96	None	9·17	0·223	0	5·00	None	9·05	0·247
5	—	,,	6·75	0·278	5	—	0·004	8·00	0·233
12	3·75	,,	7·55	0·233	12	3·65	3·55	3·76	0·303

of the polysaccharide fraction obtained from a fructose culture gave mannose, glucose, and galactose. Paper chromatography of a fructose medium indicated the presence of glycerol and erythritol as well as mannitol and the original fructose.

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558. *Heterocyclic Analogues of Fluorene: Indeno(1′ : 2′-4 : 5)-thiazoles from 2-Bromoindan-1-one.*

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Reaction of 2-bromoindan-1-one (for which an improved method of preparation is reported) with thioformamide, thioacetamide, thiobenzamide, thiourea, and potassium thiocyanate gave indeno(1′ : 2′-4 : 5)thiazole and various 2-derivatives thereof.

INVESTIGATIONS have been described [1] in which, by means of azido-reactions, derivatives of fluorene yield phenanthridines. It is intended to apply this method of synthesis of a pyridine ring in a condensed ring system to compounds analogous to fluorene but in which one or both phenylene rings of the latter are replaced by heterocycles, and as a first stage several indenothiazoles (I) have been prepared by means of the Hantzsch thiazole synthesis.

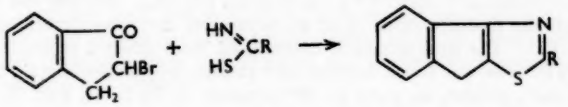
Cinnamic acid was hydrogenated and then cyclised to indan-1-one, by modifications of known procedures. Reaction with bromine and potassium chlorate,[2] applied to indanone, gave 2-bromoindan-1-one more satisfactorily than Kipping's method [3] in which the ketone reacts with bromine in acetic acid.

Hantzsch's synthesis of thiazoles,[4] involving reaction of the thiol group of an *iso*-thioamide with the >CBr group of the bromo-ketone, applied to reaction of thioformamide,

[1] Arcus and Mesley, *J.*, 1953, 178; Arcus and Coombs, *J.*, 1954, 4319; Arcus and Lucken, *J.*, 1955, 1634; Arcus, Coombs, and Evans, *J.*, 1956, 1498; Arcus, Marks, and (in part) Coombs, *J.*, 1957, 4064; Arcus and Evans, *J.*, 1958, 789.
[2] Catch, Elliott, Hey, and Jones, *J.*, 1948, 272.
[3] Kipping, *J.*, 1894, **65**, 500.
[4] Literature summarised by Wiley, England, and Behr, "Organic Reactions," Vol. VI, Wiley and Sons, New York, 1951, pp. 367—409.

thioacetamide, and thiobenzamide with 2-bromoindan-1-one, yielded indeno(1′ : 2′-4 : 5)thiazole and its 2-methyl and 2-phenyl derivatives (I; R = H, Me, and Ph).

An attempt to prepare 2-methylindeno(1′ : 2′-4 : 5)oxazole by heating 2-bromoindan-1-one with acetamide gave 2 : 2-dibromoindan-1-one; acetamide is presumed to have acted as a halogen-carrier.



(I)

With thiourea 2-bromoindan-1-one gave 2-aminoindeno(1′ : 2′-4 : 5)thiazole.[5]

2-Bromoindan-1-one with potassium thiocyanate afforded 2-thiocyanatoindan-1-one. The presence of the thiocyanato-group therein was shown by the formation of thiocyanate ion on alkaline hydrolysis. On treatment with ethanolic hydrogen chloride, the thiocyanato-ketone rearranged to 2-hydroxyindeno(1′ : 2′-4 : 5)thiazole (I; R = OH). Analogous preparations of 2-hydroxythiazoles through α-thiocyanato-ketones have been recorded.[4]

Experimental

M. p.s are corrected. Ethanol refers to the 96% alcohol.

2-Bromoindan-1-one.—A suspension of cinnamic acid (200 g.) in ethanol (200 ml.) was stirred with Raney nickel (5 g.) in the presence of hydrogen (initial pressure 80 atm.); the temperature was raised during 1½ hr. to 55°; the pressure fell to the constant value 31 atm.; 633 g. of cinnamic acid thus yielded 437 g. of β-phenylpropionic acid,[6] b. p. 117·5—118°/0·35 mm., m. p. 46°.

β-Phenylpropionic acid (20 g.), heated with polyphosphoric acid [200 g.; prepared from equal weights of phosphoric oxide and phosphoric acid (65% P_2O_5)] at 80° for 80 min., yielded indan-1-one (15·4 g.), b. p. 120—122°/15 mm., m. p. 38°. The use of polyphosphoric acid is described by Koo;[7] the procedure outlined above gave the highest yields: smaller yields were obtained by (*a*) use of commercial "tetraphosphoric acid"; (*b*) use of half the quantity of polyphosphoric acid; (*c*) as the last but with further phosphoric oxide in suspension.

To a stirred suspension of potassium chlorate (7·7 g.) in a solution of indan-1-one (50 g.) in dioxan (50 ml.) and water (20 ml.) at 77—80°, bromine (12 ml.) was added during 50 min.; the flask was illuminated by a 60-w lamp. The product was twice extracted with ether; the extract was washed with water, dried (Na_2SO_4), and on evaporation yielded crude bromoindanone (78—82 g.). Repeated recrystallisation from light petroleum (b. p. 60—80°) gave 2-bromoindan-1-one, m. p. 38·5—40°. A mixture of indan-1-one and 2-bromoindan-1-one liquefied. Separation of the bromo-ketone by distillation is much more economical: the crude product (79·8 g.) gave 2-bromoindan-1-one (57·4 g.), b. p. 110—112°/0·4 mm., f. p. 37·2°.

Indeno(1′ : 2′-4 : 5)*thiazoles*.—An ethereal solution of thioformamide was prepared according to Willstätter and Wirth.[8] The concentration was determined as follows: a portion of the solution (10 ml.) was pipetted into N-sodium hydroxide (50 ml.), and the whole was heated under reflux for 1 hr.; the ether was then distilled, and the remaining solution heated under reflux for a further hour; the resultant sodium sulphide was converted[9] into barium sulphate.

To a solution of 2-bromoindan-1-one (10·0 g.) in ether (50 ml.) heated under reflux, thioformamide (3·1 g.) in ether (70 ml.) was added during 40 min.; the whole was further heated for 1 hr., during which the hydrobromide separated as a red oil, which solidified in 3 days (9·8 g.). It (9·3 g.) was ground with excess of cold N-sodium hydroxide. (Other hydrobromides, below,

[5] King and Hlavacek, *J. Amer. Chem. Soc.*, 1950, **72**, 3722.
[6] Adkins and Billica, *ibid.*, 1948, **70**, 695.
[7] Koo, *ibid.*, 1953, **75**, 1891.
[8] Willstätter and Wirth, *Ber.*, 1909, **42**, 1911.
[9] Allen and Bishop, "Scott's Standard Methods of Chemical Analysis," Vol. I, 5th Edition, van Nostrand, New York, 1939, p. 910.

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were similarly converted into the bases.) The crude base was extracted with warm N-hydrochloric acid and the extract, on being made alkaline, gave a pink powder (4·0 g.), m. p. 65·5—66·5°, which sublimed at 80—100°/10 mm. to yield *indeno*(1′ : 2′-4 : 5)*thiazole*, colourless needles, m. p. 66·5—67° (Found: C, 69·25; H, 4·25; N, 7·8; S, 18·1. $C_{10}H_7NS$ requires C, 69·35; H, 4·05; N, 8·1; S, 18·5%).

Thioacetamide (3·6 g.) in ethanol (20 ml.) was added during 20 min. to a solution, heated under reflux, of 2-bromoindan-1-one (10·0 g.) in ethanol (20 ml.); heating was maintained for 40 min. On cooling, the hydrobromide (3·72 g.) separated, and was converted into the base (1·60 g.), m. p. 82—83°. The hydrobromide crystallised from ethanol as needles, m. p. 266—267·5° (decomp.). The base was twice distilled and yielded 2-*methylindeno*(1′ : 2′-4 : 5)*thiazole*, b. p. 120—122°/0·6 mm., prisms, m. p. 91·5—92° (Found: C, 70·7; H, 4·6; N, 7·55; S, 17·5. $C_{11}H_9NS$ requires C, 70·55; H, 4·85; N, 7·5; S, 17·1%).

Solutions of thiobenzamide [10] (m. p. 119·5°; 3·3 g.) and 2-bromoindan-1-one (5·0 g.) in ethanol (respectively 15 and 10 ml.) were mixed, and heated under reflux for 45 min. On cooling there separated the hydrobromide (5·0 g.), yellow needles, m. p. 240—242° (decomp.), from which was obtained the base (3·7 g.), m. p. 100—100·5°. Neither recrystallisation nor sublimation effected complete purification; however, distillation (bath-temp. 200—235°) of the base (1·0 g.) gave as the main fraction (b. p. 164—170°/0·1 mm.) 2-*phenylindeno*(1′ : 2′-4 : 5)-*thiazole* (0·4 g.), prisms, m. p. 101·5—102° (Found: C, 77·75; H, 4·4; N, 5·5; S, 12·45. $C_{16}H_{11}NS$ requires C, 77·1; H, 4·45; N, 5·6; S, 12·85%).

A mixture of 2-bromoindan-1-one (3·0 g.) and acetamide (0·84 g.) was fused on a steam-bath; a red colour developed; ethanol (10 ml.) was then added, and heating discontinued. After 4 hr. there separated, on shaking, from the solution which had become pale yellow, a product (0·58 g.), m. p. 120—123·5°, recrystallisation of which from ethanol yielded 2 : 2-dibromoindan-1-one, prisms, m. p. 132—133·5° (Found: C, 37·2; H, 2·45; Br, 55·2. Calc. for $C_9H_6OBr_2$: C, 37·3; H, 2·1; Br, 55·1%). Kipping [3] records m. p. 132°.

To a solution of thiourea (1·07 g.) in ethanol (5 ml.) heated under reflux, 2-bromoindan-1-one (3·00 g.) in ethanol (15 ml.) was added during 1½ hr.; heating was continued for ½ hr. The pink hydrobromide separated on cooling and, after recrystallisation from ethanol, had m. p. 260—262° (decomp.). It (4·0 g.) was converted into the base (2·5 g.), m. p. 199—203° (decomp.), which on treatment with charcoal yielded 2-aminoindeno(1′ : 2′-4 : 5)thiazole, pale violet needles, m. p. 210—211° (decomp.) (Found: C, 63·75; H, 4·2; N, 15·15; S, 16·95. Calc. for $C_{10}H_8N_2S$: C, 63·75; H, 4·3; N, 14·9; S, 17·0%). King and Hlavacek [5] record m. p. 213—214° (decomp.).

To a solution of potassium thiocyanate (1·38 g.) in ethanol (10 ml.) was added 2-bromoindan-1-one (3·0 g.) in ethanol (10 ml.), and the whole was heated under reflux for 5 min. Precipitated potassium bromide was filtered off, and from the filtrate and ethanolic washings there separated on cooling 2-*thiocyanatoindan*-1-*one* (2·4 g.), prisms (from ethanol), m. p. 91·5—92° (Found: C, 62·6; H, 3·6; N, 7·25; S, 16·1. $C_{10}H_7ONS$ requires C, 63·45; H, 3·75; N, 7·4; S, 16·95%). A portion (0·2 g.) was heated under reflux for 30 min. with potassium hydroxide (0·2 g.) in ethanol (5 ml.); the whole was cooled and filtered; acetic acid in slight excess was added to the filtrate, which was then evaporated *in vacuo*; the residue was extracted with aqueous ethanol (1 : 1), and the filtered extract gave positive tests for thiocyanate ion.

Hydrogen chloride, dried by sulphuric acid, was passed for 2 hr. through a boiling solution of 2-thiocyanatoindan-1-one (1·0 g.) in ethanol (20 ml.). From the green fluorescent solution there separated on concentration a product (0·58 g.), m. p. 210—220° (decomp.), which on recrystallisation from ethanol (charcoal) yielded 2-*hydroxyindeno*(1′ : 2′-4 : 5)*thiazole*, prisms, m. p. 228—229° (decomp.) (Found: C, 63·35; H, 3·6; N, 7·3; S, 17·1%).

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[10] Fairfull, Lowe, and Peak, *J.*, 1952, 742.

XUM

559. *The Synthesis of* vic.*-Dioximes from Symmetrical Ketones.*

By R. Belcher, W. Hoyle, and T. S. West.

Several *vic.*-dioximes have been synthesised by a simple method, which is probably of wide application. Direct bromination of ketones in aqueous acetic acid gave good yields of crude α-bromo-ketones, which on treatment with buffered hydroxylamine hydrochloride gave 25—50% yields of the dioximes of *cyclo*pentane-, *cyclo*hexane-, and 4-methyl*cyclo*hexane-1 : 2-dione, and pentane-2 : 3-dione.

vic.-Dioximes have received considerable attention as reagents for nickel,[1] and as precursors of the corresponding diamines, more particularly in the alicyclic series [2,3] where the monoketones are suitable starting materials. Several methods have been proposed for the preparation of *vic.*-dioximes,[3,6] most of which proceed through the hydroxyimino-ketone [3,4] or the diketone.[4-6] Oxidation of the mono- to the di-ketone by selenium dioxide, followed by oximation, has been recommended.[4]

Previous syntheses of *cyclo*pentane-1 : 2-dione dioxime have been unsatisfactory: Jaeger and Blumendal [2] used the glutaric–oxalic ester condensation, but it is tedious and expensive; Voter [7] obtained yields of $<10\%$ of diketone using selenium dioxide oxidation, and Acheson's [8] oxidation of 2-bromo*cyclo*pentanone to the diketone by ferric chloride has given us poor yields. The conversion of α-chloroacetone into methylglyoxime has been reported by Hantzsch and Wild [9] but later the reaction was neglected in preparative work. We found similarly that 2-bromo*cyclo*pentanone could be simultaneously oxidised and oximated to give *cyclo*pentane-1 : 2-dione dioxime, and this method was applied to the synthesis of higher homologues and pentane-2 : 3-dione dioxime.

Several workers [8-13] have prepared α-bromo-ketones by direct bromination, and we adapted Acheson's method [8] to the preparation of other α-bromo-ketones. Optimum conditions for the reactions were not investigated. When unsymmetrical ketones are brominated, two different α-bromo-ketones may be formed and purification then becomes essential. Although 2-methyl*cyclo*hexanone is not symmetrical, it is reported [12] to form 2-bromo-6-methyl*cyclo*hexanone by direct bromination, hence preparation of "3-methyl nioxime" was attempted. Because of the tendency of α-bromo-ketones to decompose on storage or on being heated [11,12] no attempt was made to purify them: any by-product present at this stage did not interfere with the isolation of the dioximes.

Several techniques for converting the α-bromo-ketones into dioximes were investigated. Hantzsch and Wild's method [9] is only applicable to the water-soluble and the more reactive members. Buffered hydroxylamine solution was used, so that the reaction temperature could be increased. With the more water-soluble 2-bromo*cyclo*pentanone and 2-bromopentan-3-one, reaction was effected by slow addition of the bromo-ketone to refluxing aqueous hydroxylamine solution; for the other bromo-ketones aqueous–methanolic hydroxylamine was used. Addition of the bromo-ketone at a rate comparable with the rate of reaction minimised the formation of tar. The optimum conditions for the

[1] Welcher, "Organic Analytical Reagents," D. Van Nostrand Co., New York, 1947, Vol. III.
[2] Jaeger and Blumendal, *Z. anorg. Chem.*, 1928, **175**, 164.
[3] Jaeger and van Dijk, *Proc. Acad. Sci. Amsterdam*, 1936, **39**, 384.
[4] Banks, Diehl, Rauh, and Smith, *J. Org. Chem.*, 1945, **10**, 199.
[5] Vander Haar, Voter, and Banks, *ibid.*, 1949, **14**, 836.
[6] Banks, Hooker, and Richard, *ibid.*, 1956, **21**, 547.
[7] Voter, Ph.D. Thesis, Iowa State Coll., Ames, Iowa, 1951.
[8] Acheson, *J.*, 1956, 4232.
[9] Hantzsch and Wild, *Annalen*, 1895, **289**, 285.
[10] Pauly, *Ber.*, 1901, **34**, 1771.
[11] Kötz, Blenderman, Kárpáti, and Rosenbusch, *Annalen*, 1913, **400**, 51.
[12] Kötz and Steinhorst, *ibid.*, 1911, **379**, 15.
[13] Schotte, *Acta Chem. Scand.*, 1951, **5**, 969.

XUM

oximations were not ascertained, but neither increase of reaction time nor a larger excess of hydroxylamine improved the yield of *cyclo*pentane-1 : 2-dione dioxime.

The reason for the formation of hydroxyimino-carboxylic acids in two of the oximation reactions is not known, but might be ascribed to preferential ring contraction, although this was not expected to occur with 2-bromo-6-methyl*cyclo*hexanone. These acids were not investigated further.

The proposed procedure eliminates the hazards and difficulties associated with the use of selenium dioxide, but precautions are necessary in the manipulation of the lachrymatory α-bromo-ketones. The preparations may be completed in one day and give yields comparable with those from other methods; with *cyclo*pentane-1 : 2-dione dioxime improved yields were obtained. The synthesis should be applicable to most symmetrical ketones and to ketones which form only one α-bromo-ketone.

Experimental

2-Bromocyclopentanone.—Bromination of *cyclo*pentanone in aqueous acetic acid by Acheson's method [8] gave the bromo-ketone in 80—90% yield.

cyclo*Pentane*-1 : 2-*dione Dioxime.*—Hydroxylamine hydrochloride (165 g.) and hydrated sodium acetate (330 g.) were refluxed in water (650 ml.), and freshly prepared 2-bromo*cyclo*pentanone (86 g.) was added dropwise during ¾ hr. After a further ½ hour's refluxing, charcoal was added and the hot solution was filtered. The light brown precipitate of dioxime was filtered off at 5°. Evaporation of the mother-liquor to 400 ml. gave a further crop from which sodium acetate was removed by cold water. The total yield of dioxime was 34 g. (50%). Two recrystallisations from water using charcoal gave colourless crystals which darkened before decomposing at 202—212° (Found: N, 21·8. Calc. for $C_5H_8O_2N_2$: N, 21·85%). M. p.s ranging from 208° to 234° have been given in the literature.[7,14] The dioxime gave a characteristic, though pH-dependent, precipitate with nickel ions (cf. Voter [7]).

*2-Bromocyclohexanone.—cyclo*Hexanone (50 g.) was dissolved in water (120 ml.) and glacial acetic acid (80 ml.); two drops of bromine were added. The solution was heated at 45—50°. When reaction had started, more bromine (total 81·6 g.) was added with vigorous stirring during 15 min. Then the mixture was cooled and neutralised to Congo-red with solid sodium carbonate. The separated bromo-ketone was washed free from acid with dilute sodium carbonate solution and then with water. Addition of anhydrous sodium sulphate, followed by filtration, gave crude 2-bromo*cyclo*hexanone as a pale yellow liquid (64·2 g., 71%).

cyclo*Hexane*-1 : 2-*dione Dioxime* (" *Nioxime* ").—Hydroxylamine hydrochloride (114 g.) and hydrated sodium acetate (228 g.) were dissolved in water (230 ml.) and methanol (200 ml.). Freshly prepared 2-bromo*cyclo*hexanone (64·2 g.) was added dropwise to the refluxing solution of hydroxylamine during 1¼ hr. Then the solution was refluxed for ¾ hr. and distilled; the distillate (200 ml.) was discarded. The residue was cooled to 0° and the precipitated sodium acetate was dissolved by addition of a small amount of water. After some hours at 0°, light pink crystals of " nioxime " (19 g., 37%) separated and were washed with benzene, then recrystallised from water; the colourless crystals (13·1 g.) had m. p. and mixed m. p. 186—188° and gave a characteristic red precipitate with nickel ions. The yield was improved by ether-extraction of the mother-liquor.

*2-Bromo-4-methyl*cyclo*hexanone.*—To 4-methyl*cyclo*hexanone (50 g.) were added two drops of bromine in water (120 ml.) and glacial acetic acid (92 ml.); the whole was heated to *ca.* 50° and the remainder of the bromine (total 74 g.) added to the stirred solution during 45 min., the temperature being kept at 35—40° by cooling. Working-up the product as for 2-bromo*cyclo*hexanone gave crude 2-bromo-4-methyl*cyclo*hexanone (66 g., 78%) as an almost water-white liquid.

4-*Methyl*cyclo*hexanone*-1 : 2-*dione Dioxime* (" 4-*Methyl Nioxime* ").—To hydroxylamine hydrochloride (119 g.) and hydrated sodium acetate (238 g.) in boiling water (240 ml.) and methanol (208 ml.), freshly prepared 2-bromo-4-methyl*cyclo*hexanone (54·4 g.) was added during 1 hr., then the solution was refluxed for a further hour and distilled until the residual liquid became turbid. It was then cooled and extracted with benzene (3 × 80 ml.). Light

[14] Riley, Morley, and Friend, *J.*, 1932, 1875.

petroleum (320 ml.; b. p. 80—100°) was added to the combined benzene extracts, and the precipitated " methyl nioxime " (11 g., 25%) was removed. Recrystallisation from water gave " methyl nioxime," m. p. 181—182° (Banks *et al.*[6] gave 181—182°), which gave a characteristic precipitate with nickel ions. The yield may be improved to 29% by continuous benzene extraction.

2-*Bromocycloheptanone.*—*cyclo*Heptanone (25 g.) was brominated as above in water (57 ml.) and glacial acetic (30 ml.) at ~60° (35·6 g. of bromine added during 25 min.). Working-up as above gave 2-bromo*cyclo*heptanone (36 g., 85%) as a pale yellow liquid.

cyclo*Heptane*-1 : 2-*dione Dioxime* (" *Heptoxime* ").—To hydroxylamine hydrochloride (25·4 g.) and hydrated sodium acetate (50·8 g.) in boiling water (50 ml.) and methanol (45 ml.) was added freshly prepared 2-bromo*cyclo*heptanone (11·6 g.) during 2¼ hr., then the solution was refluxed for 1 hr. and then 40 ml. of distillate were taken off in a vacuum. The pink semi-solid lumps which were formed were removed and washed with water. The filtrate deposited crystals which after recrystallisation from water and benzene gave an unidentified hydroxy-iminocarboxylic acid (1·9 g.), m. p. 139—140°, which gave a pale yellow precipitate on being heated with nickel ions. The pink semisolid material gave impure " heptoxime " (0·68 g., 7·2%), m. p. 171—176° (from benzene and water) (Vander Haar *et al.*[5] gave 182°). Washing with sodium carbonate solution caused little improvement in the m. p. The dioxime gave the characteristic orange-yellow precipitate with nickel ions. A considerable amount of a glutinous pink material was recovered from the reaction mixture.

Brominated 2-*Methyl*cyclo*hexanone.*—2-Methyl*cyclo*hexanone (25 g.) was brominated in water (60 ml.) and acetic acid (45 ml.) as above at *ca.* 60° (37 g. of bromine added during 15 min.). When worked up as above, this gave the crude bromo-ketone (33 g., 78%).

Oximation of Brominated 2-*Methyl*cyclo*hexanone.*—To hydroxylamine hydrochloride (36 g.) and hydrated sodium acetate (72 g.) in boiling water (72 ml.) and methanol (60 ml.), the freshly prepared bromo-ketone (16·5 g.) was added during ½ hr. and the solution refluxed for a further hour, before distillation; 60 ml. of distillate were collected and discarded. A small amount of water was added to the residue to dissolve precipitated sodium acetate, and the solution was then cooled. A small amount of tar which separated was removed. The light pink solid (7·8 g.) deposited later was filtered off and washed with ice-cold water. Recrystallisation from water gave colourless crystals of a hydroxyimino-carboxylic acid, m. p. 143—145°, which gave no reaction with nickel ions. The mother-liquor gave an orange-red precipitate with nickel ions; this nickel-active material, presumed to be the required dioxime, was almost completely extracted with ether. Concentration of the extract gave only a small amount of glutinous product.

2-*Bromopentan*-3-*one.*—To diethyl ketone (50 g.) in water (120 ml.) and acetic acid (80 ml.), bromine (93 g.) was added as described for 2-bromo*cyclo*hexanone, at 65—70°. This gave crude 2-bromopentan-3-one (82·5 g., 86%).

Ethylmethylglyoxime.—To hydroxylamine hydrochloride (31·3 g.) and hydrated sodium acetate (63 g.) in boiling water (120 ml.) was added freshly prepared 2-bromopentan-2-one (16·5 g.) during 1¼ hr. The solution, which contained an oil, was refluxed for a further hour. The boiling solution was treated with charcoal and filtered immediately. Precipitation of the product was completed at 0°; this gave colourless ethylmethylglyoxime (6 g., 46%), m. p. 172—173° (from water) (Schotte [13] gave 172—173°). The dioxime gave a characteristic orange-red precipitate with nickel ions.

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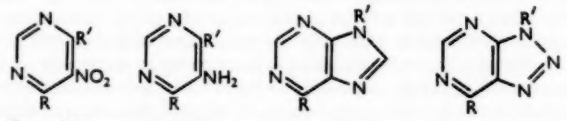
560. *The Synthesis of Kinetin and Some Related Heterocyclic Compounds.*

By R. Hull.

Ring closure of 4 : 5-diamino-6-furfurylaminopyrimidine with ethyl orthoformate and acetic anhydride has yielded the unexpected 6-furfurylaminopurine (kinetin). The isomeric 6-amino-9-furfurylpurine and kinetin are formed by ring closure of the same pyrimidine with formamide. Other purines and triazolopyrimidines are also described.

Furfuryl- and furyl-purines and -pyrimidines are of interest as analogues of ribosides and deoxyribosides in which the furanose structure is replaced by furan. Such compounds could conceivably act as antiviral agents by antagonising the formation of nucleic acids which form an integral part of virus structures, or might have interesting effects on cell metabolism.

During this investigation an attempt was made to synthesise 9-furfuryladenine (V), an analogue of adenosine. This involved the preparation of 4 : 5-diamino-6-furfurylaminopyrimidine (IV), followed by conversion of this into the purine. Theoretically ring closure



(I) — (III) (VIII) (IV) (IX) (V) — (VII) (X) (XI) (XII)

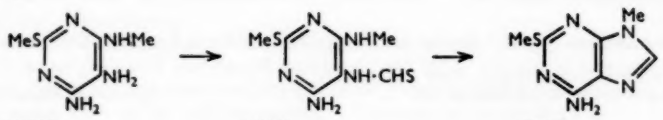
	R	R′
(I)	Cl	Cl
(II)	NH_2	Cl
(III)	NH_2	NH·C_5H_5O
(IV)	NH_2	NH·C_5H_5O

	R	R′
(V)	NH_2	C_5H_5O
(VI)	NH·C_5H_5O	H
(VII)	NAc·C_5H_5O	H
(VIII)	Cl	NH·C_5H_5O

	R	R′
(IX)	Cl	NH·C_5H_5O
(X)	—	C_5H_5O
(XI)	NH_2	C_5H_5O
(XII)	OH	C_5H_5O

C_5H_5O = furfuryl.

could occur in two ways, giving a purine substituted either by furfurylamino at position 6 (VI) or by furfuryl at position 9 (V). The ring closure of 5 : 6-diaminopyrimidines containing a substituted amino-group in position 4 has been investigated by Todd and his coworkers in experiments on the synthesis of nucleosides. They found,[1] for example, that ring closure of the methylaminopyrimidine (XIII), *via* the thioformamido-compound (XIV), gave only one product, the 9-substituted purine (XV). Later they found that a similar ring closure took place with a 4-tri-*O*-acetylribosylaminopyrimidine.[2] However, when xylose replaced the ribose portion, mixtures of the 9- and the 6-substituted purine were obtained.[3]



(XIII) (XIV) (XV)

A newer method for the synthesis of purines was suggested by the observation by Goldman, Marsico, and Gazzola[4] that 4 : 5-diaminopyrimidines on treatment with ethyl

[1] Baddiley, Lythgoe, McNeil, and Todd, *J.*, 1943, 383.
[2] Baddiley, Kenner, Lythgoe, and Todd, *J.*, 1944, 657.
[3] Baddiley, Lythgoe, and Todd, *J.*, 1944, 318; Kenner, Lythgoe, and Todd, *ibid.*, p. 652; Howard, Lythgoe, and Todd, *J.*, 1945, 556.
[4] Goldman, Marsico, and Gazzola, *J. Org. Chem.*, 1956, **21**, 599.

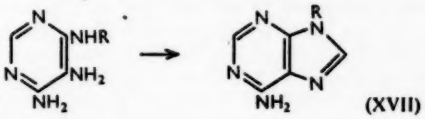
orthoformate and acetic anhydride yielded purines in good yield. In the presence of these reagents, 4 : 5-diamino-6-furfurylaminopyrimidine (IV) gave a substance, $C_{10}H_9ON_5$, which was readily soluble in aqueous sodium hydroxide, was reprecipitated from alkaline solution with acetic acid, and formed a silver salt. These properties were inconsistent with the expected 6-amino-9-furfurylpurine (V), but were in agreement with the isomeric 6-furfurylaminopurine (VI).

Great interest has centred on this compound (VI). It was originally isolated from a nucleic acid preparation,[5] during a search for a cell-division factor. The compound was shown to be 6-furfurylaminopurine,[6] and it was subsequently synthesised from 6-chloro-[7] or 6-methylthio-purine [5] and furfurylamine. It has been named " kinetin."

Comparison of the infrared absorption spectra of the compound, $C_{10}H_9ON_5$, and kinetin, as prepared by an unambiguous method, showed that they were identical. If the mild alkaline treatment was omitted after reaction of the pyrimidine (IV) with ethyl orthoformate and acetic anhydride then acetylkinetin (VII) resulted. This compound is new, since it is stated [6] that kinetin cannot be acetylated. Presumably in the ring closure of the pyrimidine (IV), acetylation of the furfurylamino-group takes place before ring closure to the purine.

Recent work on 6-(substituted amino)purines [8] suggests a widespread importance of these substances in processes of cell division, at least within the plant kingdom.

Daly and Christensen [9] have investigated the possibility of using pyrimidine intermediates for the preparation of analogues of kinetin. However, they found that cyclisation of the substituted aminopyrimidines (XVI; R = Ph, CH_2Ph, or Me) using formamide or sodium dithioformate gave only the 9-substituted purines (XVII).



(XVI) (XVII)

The behaviour of formamide on the furfurylaminopyrimidine (IV) was then investigated. A mixture of kinetin (VI) and the isomeric 9-furfurylpurine (V) resulted, easily separable by the solubility of the former in alkali. Proof of the structure (V) was obtained by preparing the compound from 6-chloro-9-furfurylpurine (X; R = Cl) and alcoholic ammonia under pressure.

Since triazolopyrimidines are of interest as antagonists of folic acid and purines in chemotherapy,[10] the diaminopyrimidine (IV) was treated with nitrous acid. Only one of the two possible isomers was obtained and this was regarded as the expected aminotriazolopyrimidine (XI). In conformity with this it was deaminated by nitrous acid at 100°, yielding the hydroxy-compound (XII).

The several pyrimidine intermediates required in the above investigation were obtained from 4 : 6-dichloro-5-nitropyrimidine (I). The furfurylaminopyrimidine (VIII) was obtained as an oil by addition of furfurylamine and triethylamine as their acetates to the dichloropyrimidine (I). Reduction with zinc dust then gave the amino-compound (IX); the same compound was also obtained from 5-amino-4 : 6-dichloropyrimidine [11] and furfurylamine. The diaminopyrimidine (IV) was obtained by a standard procedure involving stepwise nucleophilic attack on (I), to give the nitro-compound (III), followed by

[5] Miller, Skoog, Von Saltza, and Strong, *J. Amer. Chem. Soc.*, 1955, **77**, 1392.
[6] Miller, Skoog, Okumura, Von Saltza, and Strong, *ibid.*, p. 2662; 1956, **78**, 1375.
[7] Bullock, Hand, and Stokstad, *ibid.*, p. 3693.
[8] Skinner and Shive, *ibid.*, 1955, **77**, 6692; Ham, Eakin, Skinner, and Shive, *ibid.*, 1956, **78**, 2648; Skinner, Shive, Ham, Fitzgerald, and Eakin, *ibid.*, p. 5097; Sutherland and Christensen, *ibid.*, 1957, **79**, 2251; Skinner, Gardner, and Shive, *ibid.*, p. 2843.
[9] Daly and Christensen, *J. Org. Chem.*, 1956, **21**, 177.
[10] Timmis, *J. Pharm. Pharmacol.*, 1957, **9**, 84.
[11] Brown, *J. Appl. Chem.*, 1954, **4**, 72.

catalytic reduction. Early attempts to synthesise the chloropurine (X; R = Cl) were unsuccessful, owing possibly to the high reactivity of the halogen atom. In one experiment, reaction of the pyrimidine (IX) with ethyl orthoformate and acetic anhydride followed by mild treatment with alcoholic alkali to destroy the excess of reagent gave 6-ethoxy-9-furfurylpurine (X; R = OEt). Omission of the alcoholic alkaline treatment gave the halogenated purine in low yield.

Experimental

4-*Amino-6-furfurylamino-5-nitropyrimidine.*—4-Amino-6-chloro-5-nitropyrimidine [12] (3·5 g.) in dioxan (50 ml.) was added slowly during ½ hr. with stirring to furfurylamine (3·7 ml.) in dioxan (10 ml.). After a further 1½ hr. water was added and the *product* (4·6 g.) collected. It crystallised from ethanol in needles, m. p. 181—182° (Found: C, 45·8; H, 4·0; N, 30·0. $C_9H_9O_3N_5$ requires C, 46·0; H, 3·8; N, 29·8%).

4 : 5-*Diamino-6-furfurylaminopyrimidine.*—4-Amino-6-furfurylamino-5-nitropyrimidine (4·6 g.) in methanol (100 ml.) was hydrogenated over Raney nickel at room temperature and pressure. After filtration from the catalyst, the solution was evaporated. The residue (3·0 g.) crystallised from water (carbon) and gave the *aminopyrimidine* as prisms, m. p. 120—121° (Found: C, 53·0; H, 5·4; N, 34·7. $C_9H_{11}ON_5$ requires C, 52·7; H, 5·4; N, 34·1%).

6-*Furfurylaminopurine* (*Kinetin*).—4 : 5-Diamino-6-furfurylaminopyrimidine (7 g.) in ethyl orthoformate (33 ml.) and acetic anhydride (33 ml.) was heated under reflux during 1½ hr. Excess of reagent was removed under diminished pressure. 2·5N-Sodium hydroxide (70 ml.) and alcohol (35 ml.) were added to the residue, and the solution was kept at 40° during 20 min. Excess of alcohol was removed under diminished pressure and the solution was neutralised with acetic acid. The precipitated *product* (7 g.) crystallised from alcohol in leaf-shaped needles, m. p. 266° (sealed tube) (Found: C, 56·2; H, 4·4; N, 32·1. Calc. for $C_{10}H_9ON_5$: C, 55·8; H, 4·2; N, 32·6%). It was undepressed in melting point on admixture with kinetin. A solution in 0·05N-sulphuric acid gave a white precipitate with silver nitrate. The infrared absorption spectrum of the compound (Nujol smear) was identical with that of authentic kinetin.

6-(*Acetylfurfurylamino*)*purine.*—4 : 5-Diamino-6-furfurylaminopyrimidine (1·05 g.) in ethyl orthoformate (5 ml.) and acetic anhydride (5 ml.) was heated under reflux during 1½ hr. Excess of reagent was removed under reduced pressure and the residue (0·5 g.) was washed with water. Recrystallisation from alcohol gave **6-(*acetylfurfurylamino*)*purine*** as colourless needles, m. p. 151° (Found: C, 56·1; H, 4·3; N, 27·2. $C_{12}H_{11}O_3N_5$ requires C, 56·1; H, 4·3; N, 27·2%).

4-*Chloro-6-furfurylamino-5-nitropyrimidine.*—Furfurylamine (5·35 g.) and triethylamine (5·55 g.) were brought to pH 8 with 9N-acetic acid with cooling. This solution was added slowly to a stirred solution of **4 : 6-dichloro-5-nitropyrimidine** (9·7 g.) in dioxan (45 ml.) at 10—15°. After 2 hr. the mixture was added to ice-water (400 ml.), and the oil was separated and combined with the ether extract of the supernatant phase. The extracts were washed with water and dried (Na_2SO_4), and the ether was removed. Distillation of the residual oil (11·9 g.) gave a small quantity of unchanged **4 : 6-dichloro-5-nitropyrimidine** followed by the *product* as a pale brown oil (b. p. 165—170°/15 mm.) (Found: C, 42·3; H, 2·7; N, 22·0. $C_9H_7O_3N_4Cl$ requires C, 42·4; H, 2·75; N, 22·0%).

5-*Amino-4-chloro-6-furfurylaminopyrimidine.*—(*a*) 5-Amino-4 : 6-dichloropyrimidine [11] (1·7 g.) in hot dioxan (12 ml.) was added to furfurylamine (1·26 g.) and triethylamine (1·3 g.) in dioxan (3 ml.), and the whole was heated under reflux during 7 hr. The solution was set aside for 2 days, then the triethylamine hydrochloride was collected and washed with dioxan. The filtrate and washings were evaporated to dryness. The residue (2 g.), after being washed with water, crystallised from aqueous alcohol (carbon) and gave the *furfurylaminopyrimidine* as colourless needles, m. p. 137—138° (Found: C, 48·2; H, 4·0; N, 24·9. $C_9H_9ON_4Cl$ requires C, 48·1; H, 4·0; N, 24·95%).

(*b*) **4-Chloro-6-furfurylamino-5-nitropyrimidine** (0·55 g.) was added to a rapidly stirred suspension of zinc dust (2·1 g.) in water (20 ml.) at 90—95°. After 15 minutes' stirring the mixture was filtered, and the filtrates were adjusted to pH 10 with aqueous ammonia and extracted with chloroform (3 × 50 ml.). The combined extracts were dried (Na_2SO_4) and the solvent was removed. Recrystallisation of the residue from aqueous alcohol (carbon) gave 5-amino-4-chloro-6-furfurylaminopyrimidine as needles, m. p. 136°, identical with the above.

[12] Boon, Jones, and Ramage, *J.*, 1951, 96.

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6-Chloro-9-furfurylpurine.—5-Amino-4-chloro-6-furfurylaminopyrimidine (2·0 g.) in acetic anhydride (8 ml.) and ethyl orthoformate (8 ml.) was heated under reflux during 3 hr. Excess of reagent was carefully removed under diminished pressure. Trituration with ice-cold aqueous alcohol and storage gave the *purine* (0·25 g.; m. p. 96—97°) which crystallised from light petroleum (b. p. 80—100°) as prisms, m. p. 97—99° (Found: C, 51·4; H, 2·9; N, 24·0. $C_{10}H_7ON_4Cl$ requires C, 51·2; H, 3·0; N, 23·9%).

Condensation of Formamide with 4 : 5-Diamino-6-furfurylaminopyrimidine.—4 : 5-Diamino-6-furfurylaminopyrimidine (5·0 g.) and formamide (27 ml.) were heated under gentle reflux for 15 min. Ice-water was added to the cooled mixture, and the solid (3·8 g.; m. p. 176—180°) was extracted with 2N-sodium hydroxide (20 ml.). 6-Furfurylaminopurine (kinetin) [1·0 g.; m. p. 263—264° (sealed tube)] separated when this filtrate was neutralised with acetic acid. The alkali-insoluble material (1·65 g.; m. p. 188—189°) crystallised from water (carbon), to give *6-amino-9-furfurylpurine* as needles, m. p. 191—192° (Found: C, 55·9; H, 4·4; N, 33·2. $C_{10}H_9ON_5$ requires C, 55·8; H, 4·2; N, 32·6%). Basification of the original aqueous formamide filtrates gave a further quantity (0·95 g.; m. p. 188—189°) of 6-amino-9-furfurylpurine.

6-Amino-9-furfurylpurine (Second Method).—6-Chloro-9-furfurylpurine (0·5 g.) was heated in a Carius tube with alcoholic ammonia (20 ml., saturated at 0°) at 135° during 5 hr. After evaporation the residue (0·4 g.) crystallised from water in prismatic needles, m. p. 191—192°, identical with 6-amino-9-furfurylpurine prepared as above.

6-Ethoxy-9-furfurylpurine.—6-Chloro-9-furfurylpurine (0·1 g.) was suspended in 2N-sodium hydroxide (1 ml.) and alcohol (1 ml.), and the mixture was heated at 40° during 10 min. A solution was formed, and later the precipitated *product* (0·1 g.) was filtered from the cooled mixture. Crystallisation from water gave the purine as prismatic needles, m. p. 118° (Found: C, 58·9; H, 5·0; N, 22·8. $C_{12}H_{12}O_2N_4$ requires C, 59·0; H, 4·95; N, 22·95%).

6-Amino-1′-furfuryl-1′ : 2′ : 3′-triazolo(5′ : 4′-4 : 5)pyrimidine.—Sodium nitrite (0·47 g.) in water (3 ml.) was added to a solution of 4 : 5-diamino-6-furfurylaminopyrimidine (1·05 g.) in acetic acid (20 ml.) at 10°. After 15 min. the solution was diluted with water, and the *triazolopyrimidine* (0·85 g.) collected. It crystallised from alcohol in needles, m. p. 237° (Found: C, 49·8; H, 3·8; N, 38·6. $C_9H_8ON_6$ requires C, 50·0; H, 3·7; N, 38·9%). A solution of the compound in dilute aqueous sulphuric acid did not form a silver salt with silver nitrate. The compound was insoluble in dilute aqueous alkali.

The triazolopyrimidine (0·5 g.) was dissolved in water (20 ml.) containing sulphuric acid (2 g.) at 45—50°; sodium nitrite (1 g.) in water (5 ml.) was added and the mixture boiled for about 3 min. The product, which separated on cooling and scratching, recrystallised from alcohol and gave *6-hydroxy-1′-furfuryl-1′ : 2′ : 3′-triazolo(5′ : 4′-4 : 5)pyrimidine* as pale yellow plates, m. p. 226—227° (decomp.) (Found: C, 49·6; H, 3·5; N, 32·4. $C_9H_7O_2N_5$ requires C, 49·75; H, 3·2; N, 32·25%), soluble in N-sodium hydroxide.

I am grateful to Mr. K. Jones for technical assistance.

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561. *Attempts to Prepare Optically Active Tervalent Nitrogen Compounds. Part III.* Attempted Resolution of 6-Substituted 1 : 9-Phenylenecarbazoles (3-Substituted Indolo[3,2,1-jk]carbazoles).*

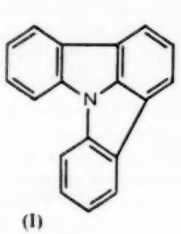
By C. Buchanan and S. Horwood Tucker.

Improved methods for preparation of 6-carboxy-, 6-methoxycarbonyl-, and 6-methyl-1 : 9-phenylenecarbazole are submitted. Optical resolution of the acid by means of its alkaloidal salts, and of the 6-methoxycarbonyl and the 6-methyl compound by means of complexes with (−)-α-(2 : 4 : 5 : 7-tetranitro-9-fluorenylideneamino-oxy)propionic acid failed. 6-Methyl-1 : 9-phenylenecarbazole was examined for unstable optical activity by dissolution in ethyl (+)-tartrate, with negative results.

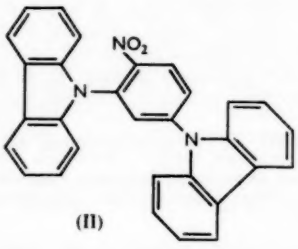
6-Bromo-1 : 9-phenylenecarbazole has been synthesised; the nature of a by-product is discussed.

Attempts at optical resolution of 1 : 9-phenylenecarbazole-3 : 6-dicarboxylic acid (indolo[3,2,1-*jk*]carbazole-6 : 9-dicarboxylic acid) by means of alkaloids failed owing to the instability of the salts in solution.[1] Similar results have now been obtained in attempts to form salts of 1 : 9-phenylenecarbazole-6-carboxylic acid (I; R = CO_2H).† The methohydroxides of alkaloids [2] similarly gave negative results. The methyl ester (I; R = CO_2Me) of the monocarboxylic acid and 6-methyl-1 : 9-phenylenecarbazole (I; R = Me) gave complexes with Newman and Lutz's compound, (−)-α-(2 : 4 : 5 : 7-tetranitro-9-fluorenylideneamino-oxy)propionic acid,[3] but no resolution could be effected. Crystallisation of 6-methyl-1 : 9-phenylenecarbazole from ethyl (+)-tartrate [4] also failed to disclose optical activity.

The 6-derivatives (I; R = Me, CO_2H, CO_2Me) have been prepared before,[1]† but in such poor yield that further work with them was impracticable. Improved methods starting from carbazole [1] and from 1-nitrocarbazole [5] are described in the Experimental section.



(I)



(II)

6-Bromo-1 : 9-phenylenecarbazole (I; R = Br) has been synthesised from carbazole, 2 : 5-dibromonitrobenzene, potassium carbonate, and copper bronze at 244°. When, however, one or more mols. of carbazole per mol. of 2 : 5-dibromonitrobenzene were used, a bromine-free by-product was obtained. It is suggested that this compound may be 2 : 4-dicarbazolyl-1-nitrobenzene (II), produced by nucleophilic attack by the 9-carbazolyl anion on the carbon atom *para* to the nitro-group in the initially formed 9-(4-bromo-2-nitrophenyl)carbazole, concomitant displacement of bromine by hydride ion taking

* Part II, *J.*, 1943, 659.

† Previously [1] these compounds had been ambiguously named as 4'-derivatives.

[1] Dunlop and Tucker, *J.*, 1939, 1945.
[2] Major and Finkelstein, *J. Amer. Chem. Soc.*, 1941, **63**, 1368.
[3] Newman and Lutz, *ibid.*, 1956, **78**, 2469.
[4] Buchanan and Graham, *J.*, 1950, 500.
[5] Cf. Preston and Tucker, *J.*, 1943, 659.

place. This is analogous to the action of nitrobenzene on carbazole in the presence of caustic alkali.[6] The novel suggestion that such replacements may involve a benzyne intermediate [7] might apply here, but the directive influence of the nitro-group should then favour formation of the 1 : 4-dicarbazolyl-2-nitrobenzene. This compound (II) was also prepared (78% yield) by reaction of 9-(4-bromo-2-nitrophenyl)carbazole (assumed to be the intermediate above) and carbazole. Attempts to prepare it by heating carbazole and 9-*o*-nitrophenylcarbazole with potassium carbonate and a trace of copper at 244° for 5 hours or potassium hydroxide and a trace of copper at 155° for 1 hr. failed.

The ultraviolet absorption spectra are summarised in the Table. The complete curves of the 9-substituted carbazoles closely resemble one another; similarly, those graphs of the 6-substituted 1 : 9-phenylenecarbazoles are practically superposable. But, as would be expected, the two series exhibit marked differences, providing a decisive criterion of ring closure.

Ultraviolet absorption spectra (λ *in* mμ) *of ethanol solutions.*

1 : 9-*Phenylenecarbazoles.*								
Unsubst.	$\lambda_{max.}$	237	267	283	291	307	319	361
	log ε	4·78	4·53	4·56	3·96	3·84	3·91	3·95
6-Methyl	$\lambda_{max.}$	235	270	284	296	310	322	366
	log ε	4·78	4·58	4·46	3·95	3·89	3·92	3·82
6-Bromo	$\lambda_{max.}$	234 [b]	273	285	297	309	322	368
	log ε	4·72	4·65	4·49	4·09	3·89	3·96	3·94
6-Methoxycarbonyl [a]	$\lambda_{max.}$	—	—	285	—	—	—	361
	log ε	—	—	3·71	—	—	—	3·25
6-Ethoxycarbonyl [a]	$\lambda_{max.}$	—	—	285	—	—	—	361
	log ε	—	—	3·68	—	—	—	3·26
Carbazoles.								
Unsubst. [c,d]	$\lambda_{max.}$	234	245	257	293	324	337	
	log ε	4·58	4·36	4·27	4·18	3·51	3·47	
9-Phenyl	$\lambda_{max.}$	239	—	—	292 [e]	326	340	
	log ε	4·71	—	—	4·29	3·57	3·63	
9-C_6H_4·CO_2Et-*p*	$\lambda_{max.}$	—	—	—	293	327	339	
	log ε	—	—	—	3·23	3·19	3·16	

[a] In $CHCl_3$ (measured by Mr. G. Ferguson). [b] Also an exceptional max. at 240 mμ (log 4·73). [c] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley & Sons, New York, 1951, No. 293. [d] The 9-methyl, 9-*iso*propyl, 9-*p*-chlorophenyl, 3-chloro-, 3-bromo-, 3-bromo-9-methyl, 3-bromo-9-ethyl, and 3-iodo-9-methyl analogues had almost the same $\lambda_{max.}$ as the 9-phenyl compound and very similar ε. [e] Also an exceptional max. at 287 mμ (log ε 4·20).

Unsuccessful attempts have been made to condense carbazole with 2-chloro-1 : 3-benzene.[8]

This line of research has now been abandoned.

Experimental

Attempted Optical Resolutions.—1 : 9-Phenylenecarbazole-4′-carboxylic acid failed to form isolatable salts with (−)-brucine, (−)-quinine, (+)-cinchonine, or (+)-1-phenylethylamine in acetone. The acid appeared to form a salt with (−)-quinine methohydroxide,[2] since it dissolved readily in a warm aqueous-alcoholic solution of one equivalent of the base, but, on cooling, an uncrystallisable oil, presumably the salt, separated. Evaporation of the solution to dryness resulted in dissociation. Addition of dioxan or benzene to a solution of the salt in ethanol gave the acid, fractional precipitation yielding samples with zero rotation in pyridine. Similar results were obtained with the methohydroxides of (+)-cinchonine and (+)-quinidine.[2]

4′-Methyl-1 : 9-phenylenecarbazole and methyl 1 : 9-phenylenecarbazole-4′-carboxylate gave molecular complexes with (−)-α-(2 : 4 : 5 : 7-tetranitro-9-fluorenylideneamino-oxy)-propionic acid in acetic acid, but substances recovered from the complexes and from the acetic acid mother-liquors showed no rotation in chloroform.

[6] G. and M. de Montmollin, *Helv. Chim. Acta*, 1923, **6**, 94; cf. Nelmes and Tucker, *J.*, 1933, 1523.
[7] Roberts, Simmons, Carlsmith, and Vaughan, *J. Amer. Chem. Soc.*, 1953, **75**, 3290; *Ann. Reports*, 1956, **53**, 192.
[8] Gunstone and Tucker, *J. Appl. Chem.*, 1952, **2**, 204.

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4'-Methyl-1 : 9-phenylenecarbazole crystallised from ethyl (+)-tartrate in an inactive condition.

1-*Nitrocarbazole*.—To carbazole (8·35 g.) in acetic anhydride (50 ml.), a mixture of concentrated nitric acid (3·5 ml.) and acetic anhydride (5 ml.), cooled to 0°, was added, the temperature being kept at 10—15°. The mixture was heated to 80°, and there maintained for 10 min., then concentrated to half its bulk. A drop of concentrated sulphuric acid in acetic anhydride (1 ml.) was added, and the mixture boiled, with vigorous shaking, until solid separated. It was allowed to cool and crystallise. 9-Acetyl-3-nitrocarbazole was removed and washed with acetic acid or acetone, in which it is practically insoluble: crystallised from nitromethane, it had m. p. 237—238°. The filtrate was poured into hot water (300 ml.), the cold mixture was filtered, the solid dried and dissolved in benzene, and the solution distilled until all water had passed over, then chromatographed on alumina (10 × 2·5 cm.) previously heated to 300° for 3 hr.; the first eluate gave 1-nitrocarbazole (1·12 g., 9%), m. p. 187°. This method has no advantage over others.[9]

Synthesis of 6-Methyl-1 : 9-phenylenecarbazole (I; R = Me).—*Route A, from carbazole* (with N. C. Kirk). Carbazole (8·35 g.), 4-bromo-3-nitrotoluene (27 g., 150 % excess), potassium carbonate (8·4 g.), and copper bronze (0·15 g.) were heated at 244° (diethylene glycol vapour)[10] for 80 min., the melt was extracted with boiling benzene, the solution steam-distilled to remove benzene and excess of bromonitrotoluene, and the remaining tar extracted with ethanol; crystals grew therefrom very slowly. Recrystallisation from acetic acid gave orange prisms (*ca.* 60%), m. p. 93—94° (lit., 104—106°) of 9-(4-methyl-2-nitrophenyl)carbazole (Found: C, 75·6; H, 4·4; N, 9·1. Calc. for $C_{19}H_{14}O_2N_2$: C, 75·5; H, 4·7; N, 9·3%).

This nitro-compound (2·2 g.) was reduced by hydrogen and Raney nickel in ethanol (*ca.* 2 hr.) to give cream prisms (from ethanol), m. p. 116—118° (1·83 g., 90%), of the amine (Found: C, 83·8; H, 6·0. Calc. for $C_{19}H_{16}N_2$: C, 83·8; H, 5·9%). Final darker crops were best obtained by slow evaporation.

The amine (2·72 g.) dissolved in a hot mixture of acetic acid (10 ml.), concentrated sulphuric acid (12 ml.), and water (50 ml.). The solution after being quickly cooled, with shaking, to *ca.* 20° was treated, all at once, with sodium nitrite (0·76 g., 10% excess) in water (10 ml.). The deep red solution was diluted with water (80 ml.) and treated with sulphamic acid, copper bronze added, and the whole cautiously heated until effervescence was vigorous: it was then heated on a boiling-water bath, with occasional swirling, until the liquid portion was colourless (45 min.). After cooling, the salmon-coloured solid was removed, washed, and boiled with benzene, the solution filtered from copper, water removed by distillation in benzene, and the residual oil chromatographed in ligroin (b. p. 60—80°) on alumina (10 × 2 cm.). The colourless eluate (violet in ultraviolet light) gave 6-methyl-1 : 9-phenylenecarbazole, m. p. 110—112° (2·14 g., 84%), as needles having a faint violet fluorescence. No phenolic material could be detected in the benzene solution. Use of benzene in place of ligroin for chromatography gave a brown eluate. 6-Methyl-1 : 9-phenylenecarbazole gave a deep scarlet 2 : 4 : 7-*trinitrofluorenone complex* (from acetic acid), softening at 193°, melting at 200° (Found: C, 67·3; H, 3·1; N, 10·0. $C_{19}H_{13}N,C_{13}H_5O_7N_3$ requires C, 67·4; H, 3·2; N, 9·8%).

Route (B), from 1-nitrocarbazole. 1-Nitrocarbazole (0·8 g.), *p*-iodotoluene (6 g.), anhydrous potassium carbonate (0·8 g.), and copper bronze (0·01 g.) were heated under reflux for 6 hr.; the excess of *p*-iodotoluene was removed by distillation (3·5 g. recovered), the residue extracted with boiling acetone, the extract steam-distilled to remove the rest of the *p*-iodotoluene, the residue extracted with benzene, and the dried solution chromatographed on alumina (5 × 1·5 cm.). The eluate gave a yellow solid which after crystallisation from benzene (charcoal) and then from methyl acetate gave canary-yellow octahedra of 1-*nitro*-9-p-*tolylcarbazole*, m. p. 159—160° (0·74 g., 65%) (Found: C, 75·7; H, 4·6; N, 9·1. $C_{19}H_{14}O_2N_2$ requires C, 75·5; H, 4·7; N, 9·3%). When the reaction mixture was heated for only 3 hr., the yield was reduced to 58%.

The above nitro-compound (3·02 g.) was hydrogenated in benzene (50 ml.) in presence of Raney nickel (2 g.) and ethanol (10 ml.) until 820 ml. of hydrogen had been absorbed (theor., 672 ml.). The *amine* (2·38 g., 87%) was purified with difficulty, but by crystallisation from light petroleum (b. p. 80—100°), then from methanol and from ethanol; it was obtained in pale green needles, m. p. 131—132° (Found: C, 83·8; H, 6·0; N, 10·3. $C_{19}H_{16}N_2$ requires

[9] Preston, Tucker, and Cameron, *J.*, 1942, 500.
[10] Tucker, *J. Chem. Educ.*, 1953, **30**, 634.

C, 83·8; H, 5·9; N, 10·3%). The *acetyl derivative*, m. p. 212—213° (formed by acetic anhydride in benzene), crystallised in pale brown stout prisms from acetic acid (Found: C, 80·0; H, 5·9; N, 8·7. $C_{21}H_{16}ON_2$ requires C, 80·2; H, 5·8; N, 8·9%).

Cyclisation of the above amine was accomplished in *ca.* 41% yield, as for the analogous cyclisation from 9-(2-amino-4-methylphenyl)carbazole to give, as before, 6-methyl-1 : 9-phenylenecarbazole, m. p. and mixed m. p. 110—112°.

Synthesis of 1 : 9-*Phenylenecarbazole-6-carboxylic Acid from* 1-*Nitrocarbazole.*—*Methyl* 1-*nitro*-9-*phenylcarbazole-4'-carboxylate* (with E. THOMSON, B.Sc.). A mixture of 1-nitrocarbazole (2·12 g., 0·01 mole), methyl *p*-iodobenzoate (7·8 g., excess), anhydrous potassium carbonate (0·7 g.), and copper bronze (0·04 g.) were heated in the vapour of boiling methyl salicylate [10] (b. p. 223°) with continuous stirring with a spiral copper wire. After 2 hr. another addition of potassium carbonate (0·7 g.) and copper (0·04 g.) was made, and heating continued for 4 hr. The melt was extracted with hot water, the filtrate rendered acid with hydrochloric acid, and the precipitated *p*-iodobenzoic acid (1·14 g.; m. p. 264°) removed. A benzene extract of the original melt, on steam-distillation, gave benzene and methyl *p*-iodobenzoate (3·5 g.). The undistilled red residue was filtered, dried, dissolved in benzene, and chromatographed on alumina (20 × 1·5 cm.). On elution with benzene, a canary-yellow band developed: the first 300 ml. of eluate, after evaporation to dryness and crystallisation of the residue from ethanol, gave the main bulk (2·00 g.), but continued elution (750 ml.) gave more (0·46 g.) *methyl* 1-*nitro*-9-*phenylcarbazole-4'-carboxylate*, m. p. 170—171° (total, 2·46 g., 78%) (Found: C, 69·3; H, 4·3; N, 8·2. $C_{20}H_{14}O_4N_2$ requires C, 69·35; H, 4·1; N, 8·1%). When heating was for only 3 hr., unchanged 1-nitrocarbazole was recovered. It appeared as a deep red-brown band on the chromatogram and was eluted after methyl 1-nitro-9-phenylcarbazole-4'-carboxylate. Crystallisation of the crude 1-nitrocarbazole from benzene separated it from the much more soluble carboxylate. The reverse is true when ethanol is used. Methyl 1-nitro-9-phenylcarbazole-4'-carboxylate normally crystallises in stout pale yellow prisms, but these soon became superficially golden-yellow: long pale green needles often separated from cold solutions. The m. p. of the two forms, and of a mixture, was 170—171°. The needles slowly changed to the yellow prisms. The forms appear to be polymorphs.

Methyl 1-*amino*-9-*phenylcarbazole-4'-carboxylate.* The nitro-ester (2·08 g.) dissolved in benzene (20 ml., which had been stored over Raney nickel) was reduced by hydrogen in presence of Raney nickel (2 g. in 10 ml. of ethanolic suspension) in 2 hr. Hydrogen (462 ml.) was absorbed, in excess of that required by theory (402 ml.). The mixture was boiled and filtered, and the nickel extracted with boiling ethanol. The combined liquors were evaporated to small bulk, to give pale green needles (later crops, pale brown plates) of pure *methyl* 1-*amino*-9-*phenylcarbazole-4'-carboxylate*, m. p. 173—174° (1·81 g., 95%). Crystallisation from methanol gave a mixture of faintly yellow needles and stout yellow-ochre prisms. Both, and a mixture, had m. p. 173—174° (Found: C, 76·2; H, 5·0; N, 8·9. $C_{20}H_{16}O_2N_2$ requires C, 75·9; H, 5·1; N, 8·9%). The amine, when boiled with acetic anhydride in benzene, gave the *acetyl derivative* as thin rods (from ethanol), m. p. 202—204° (Found: C, 73·65; H, 5·1; N, 8·0. $C_{22}H_{18}O_3N_2$ requires C, 73·7; H, 5·1; N, 7·8%).

In one hydrogenation of methyl 1-nitro-9-phenylcarbazole-4'-carboxylate, with Raney nickel and ethanol but no benzene, absorption of hydrogen was less than the theoretical: yellow-ochre short prisms, m. p. 140—141°, were isolated from ethanol, consisting probably of *methyl* 1-*hydroxyamino*-9-*phenylcarbazole-4'-carboxylate* (Found: C, 72·1; H, 4·7; N, 8·9. $C_{20}H_{16}O_3N_2$ requires C, 72·3; H, 4·8; N, 8·4%).

Methyl 1 : 9-*Phenylenecarbazole-6-carboxylate* (I; R = CO_2Me). The amino-9-phenylcarbazole-4'-carboxylate (0·316 g.) in a mixture of concentrated sulphuric acid (2 ml.) and water (8 ml.) was diazotised by rapid addition of sodium nitrite (1·05 g., 50% excess) in water (15 ml.) without cooling. The deep red solution was diluted with water (15 ml.) (apparently necessary for completion of diazotisation), sulphamic acid was added to destroy excess of nitrite, then copper bronze, and the mixture boiled gently for 30 min. The hot suspension of red and yellow flocculent precipitates was extracted with benzene, copper was removed, and the benzene extract was shaken with 10% aqueous potassium hydroxide. The alkaline solution contained chiefly phenolic by-products: in only a few experiments could carboxylic acid be separated. The benzene extract was distilled until all the water had been carried over, and the concentrate was then chromatographed on alumina (8 × 1·5 cm.) and eluted with benzene. Various colours (in ultraviolet light) developed, but were due to impurities. After the first

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runnings (*ca.* 50 ml.) had been discarded, most of the *ester* was obtained in the next 250 ml. of eluate. Crystallisation from light petroleum (b. p. 80—100°) gave needles, m. p. 163—164° (0·10 g., 33%) (Found: C, 80·2; H, 4·1; N, 4·9. $C_{20}H_{13}O_2N$ requires C, 80·2; H, 4·4; N, 4·7%).

1 : 9-Phenylenecarbazole-6-carboxylic acid (I; R = CO_2H) was prepared by boiling this ester (1·05 g.) with 10% aqueous potassium hydroxide (25 ml.) and ethanol (30 ml.) for 1 hr. The clear liquor, poured into hot water (1 l.) (the potassium salt of the carboxylic acid is only slightly soluble), gave a nearly clear solution which with excess of concentrated hydrochloric acid gave a voluminous precipitate (*ca.* 100%). This acid crystallised from anisole in needles, softening at 335°, melting at 342° (Found: C, 79·8; H, 3·9; N, 4·9. Calc. for $C_{19}H_{11}O_2N$: C, 80·0; H, 3·9; N, 4·9%). The 2 : 4 : 7-*trinitrofluorenone complex*, orange crystals from acetic acid, softened at 280° and melted much higher: it dissociated on attempted crystallisation (Found: C, 63·7; H, 2·6; N, 9·2. $C_{19}H_{11}O_2N,C_{13}H_5O_7N_3$ requires C, 64·0; H, 2·7; N, 9·3%). Esterification with ethanolic hydrogen chloride gave the *ethyl ester* (I; R = CO_2Et), needles [from 1 : 1-benzene–light petroleum (b. p. 80—100°)], m. p. 173—174° (Found: C, 80·5; H, 4·9; N, 4·5. $C_{21}H_{15}O_2N$ requires C, 80·5; H, 4·8; N, 4·5%).

Oxidation of 6-*Methyl*-1 : 9-*phenylenecarbazole to* 1 : 9-*Phenylenecarbazole*-6-*carboxylic Acid.*—6-Methyl-1 : 9-phenylenecarbazole (0·43 g.) and potassium hydroxide (0·05 g.) in water (2 ml.) and pyridine (10 ml.) were treated at the b. p. with potassium permanganate (*ca.* 0·75 g.) in portions during 3 hr. Excess of dilute sulphuric acid containing sulphurous acid was added, and the white precipitate was filtered off, washed, dried, and extracted with ligroin (b. p. 60—80°) to remove unchanged methyl compound (0·05 g.). The residue was pure 1 : 9-phenylenecarbazole-6-carboxylic acid (0·41 g., 84%). A nearly theoretical yield was obtained by using relatively more (50%) of solvents and reagents, and heating for 7·5 hr. 6-Methyl-1 : 9-phenylenecarbazole was unaffected when boiled in acetone with potassium permanganate.

The acid was decarboxylated by copper bronze.[1] The benzene extract of the melt was chromatographed on alumina, and the product, isolated in the usual way, crystallised from methanol–acetone (2 : 1 v/v). The 1 : 9-phenylenecarbazole had m. p. and mixed m. p. 135—137°.

Synthesis of 6-*Bromo*-1 : 9-*phenylenecarbazole* (I; R = Br) (with J. M. Couper, B.Sc.).—Carbazole (11·7 g., 0·07 mole), 2 : 5-dibromonitrobenzene (39·3 g., 0·14 mole), anhydrous potassium carbonate (20 g., 0·14 mole), and copper bronze (0·1 g.) were stirred together at 244° for 1 hr.[10] The product was extracted with boiling acetone, the concentrated solution poured into dilute hydrochloric acid, and the precipitated red oil washed with water, and crystallised by dissolving in a small amount of acetone and adding boiling methanol, as orange prisms of 9-(4-*bromo*-2-*nitrophenyl*)*carbazole* (12·8 g., 50%), m. p. 152—154° (Found: C, 59·0; H, 3·2; N, 7·8. $C_{18}H_{11}O_2N_2Br$ requires C, 58·9; H, 3·0; N, 7·6%). The yield was from 39% after 0·25 hour's heating to 54% after 6 hours.

When copper was omitted, a charred mass was obtained under various conditions.

The isolation of a compound, m. p. 220°, is described below.

The foregoing nitro-compound (2 g.) in boiling glacial acetic acid (100 ml.) was treated with activated zinc (6 g., activated with dilute hydrochloric acid). Colour was discharged in 10 min., but refluxing was continued for 1 hr. The liquid decanted from unused zinc, was poured into water, giving a white precipitate containing zinc; this was dissolved in acetic acid and poured into excess of diluted hydrochloric acid (1 part of concentrated acid and 10 parts by vol. of water). The precipitate, washed with water and dried, was pale brown and had m. p. 93—95° (1·3 g., 65%). Recrystallisation was extremely difficult, usually only oils being obtained. Ethanol, or ethanol containing a trace of water, gave the *amine* as rosettes of prisms, softening at 95°, melting at 100° (Found: C, 64·1; H, 3·9; N, 8·25. $C_{18}H_{13}N_2Br$ requires C, 64·1; H, 3·9; N, 8·3%).

Reduction with hydrogen in presence of Raney nickel in ethanol gave the amine but, again, the product could not be readily crystallised; there was evidence that it contained a bromine-free substance, possibly 9-*o*-aminophenylcarbazole (see below). Reduction in methanol gave a solid amine which could not be recrystallised. This product gave a 2 : 4 : 7-*trinitrofluorenone complex* as deep red prisms, m. p. 198—215°, but attempts to crystallise it from glacial acetic acid gave the trinitrofluorenone. The amine gave a *picrate*, softening at 80°, m. p. 99°, as orange prisms from methanol (Found: C, 45·4; H, 2·6; N, 14·25. $C_{18}H_{13}N_2Br,2C_6H_3O_7N_3$ requires C, 45·3; H, 2·4; N, 14·1%). Since the substance evidently dissociates the m. p. is unreliable. During crystallisation yellow and orange crystals separated. The amine with

acetic anhydride and benzene gave the ***acetyl derivative*** as leaflets (from ethanol), m. p. 217—219° (Found: C, 63·2; H, 4·1. $C_{20}H_{15}ON_2Br$ requires C, 63·3; H, 4·0%). This was obtained also by reduction of the nitro-compound by zinc, acetic acid, and acetic anhydride. Reduction of the nitro-compound by zinc, ammonium chloride, and ethanol gave no useful result.

The oily amine (0·9 g.) obtained by hydrogen and Raney nickel in ethanol was treated in glacial acetic acid (10 ml.), concentrated sulphuric acid (5 ml.), and water (10 ml.) with sodium nitrite (2 g.) in water (2—3 ml.), without external cooling. The deep scarlet solution was diluted with water (10 ml.), sulphamic acid and then copper bronze were added, and the solution was slowly heated to the b. p. and kept thereat for 10 min. The black pasty mass obtained was dissolved in benzene, water removed by distilling off most of the benzene, and the dry solution chromatographed on alumina. After removal of a pale blue (ultraviolet light) band, elution (*ca.* 250 ml.) of a continuous purple zone gave, in the usual way, leaflets (from ethyl acetate containing a drop of ethanol) of **6-*bromo*-1 : 9-*phenylenecarbazole*** (0·07 g.), m. p. 144—145° (Found: C, 67·7; H, 3·3; N, 4·3. $C_{18}H_{10}NBr$ requires C, 67·5; H, 3·15; N, 4·4%). It gave a scarlet **2 : 4 : 7-*trinitrofluorenone complex*** (from acetic acid), m. p. 181—182° (Found: C, 58·45; H, 2·5; N, 8·7. $C_{18}H_{10}NBr,C_{13}H_5O_7N_3$ requires C, 58·6; H, 2·4; N, 8·8%). It also gave a **1 : 3 : 5-*trinitrobenzene complex*** (from acetic acid), golden-yellow needles, m. p. 156—158° (Found: C, 54·3; H, 2·6. $C_{18}H_{10}NBr,C_6H_3O_6N_3$ requires C, 54·1; H, 2·45%). Filtrates after isolation of 6-bromo-1 : 9-phenylenecarbazole, when treated with picric acid, gave a small amount of a red picrate, softening at 140°, m. p. 165°, which contained no bromine, and appeared to be the picrate (m. p. 165—169°) of 1 : 9-phenylenecarbazole (Found: C, 61·0; H, 3·1; N, 12·0. Calc. for $C_{18}H_{11}N,C_6H_3O_7N_3$: C, 61·3; H, 3·0; N, 11·9%). The 1 : 9-phenylenecarbazole is probably derived from 9-*o*-aminophenylcarbazole produced during the preceding reduction. For comparison, the **2 : 4 : 7-*trinitrofluorenone complex*** of 1 : 9-phenylenecarbazole was prepared in acetic acid forming scarlet needles, m. p. 198—199° (Found: C, 66·9; H, 2·8; N, 10·0. $C_{18}H_{11}N,C_{13}H_5O_7N_3$ requires C, 66·9; H, 2·9; N, 10·1%).

2 : 4-*Dicarbazolyl*-1-*nitrobenzene* (II).—When in the preparation of 9-(4-bromo-2-nitrophenyl)-carbazole, 1 mol. or more of carbazole to 2 : 5-dibromonitrobenzene was used at 244° during 6 hr., there were obtained at first (before removal of the dibromonitro-compound) from the acetone extract, scarlet plates, m. p. 220°. These were better prepared by the action of carbazole on 9-(4-bromo-2-nitrophenyl)carbazole: carbazole (1·0 g.), 9-(4-bromo-2-nitrophenyl)-carbazole (0·9 g.), anhydrous potassium carbonate (0·5 g.), and copper bronze (0·2 g.) were heated at 244° for 5 hr. The boiling acetone extract gave practically pure, scarlet diamond-shaped plates of **2 : 4-*dicarbazyl*-1-*nitrobenzene***, which, after chromatography in benzene on alumina and crystallisation from benzene, had m. p. 220° (0·87 g., 78%) (Found: C, 79·4; H, 4·0; N, 9·1. $C_{30}H_{19}O_2N_3$ requires C, 79·45; H, 4·2; N, 9·3%). When, in the above experiment, the amount of copper was doubled, the yield was reduced to 29%: it is difficult to understand why copper should thus influence the reaction.

9-p-*Bromophenylcarbazole*.—Carbazole (1·12 g.), *p*-bromoiodobenzene (2·83 g.), anhydrous potassium carbonate (1·5 g.), and copper bronze (0·01 g.) were heated at 244° for 6 hr. The acetone extract, poured into dilute hydrochloric acid, gave a brown solid which crystallised from benzene–ligroin (b. p. 60—80°) in thick rectangular plates, then from methyl cyanide in pale brown prisms, m. p. 146—147° (Found: C, 67·0; H, 3·9; N, 4·15. $C_{18}H_{12}NBr$ requires C, 67·1; H, 3·8; N, 4·35%). A mixture with 6-bromo-1 : 9-phenylenecarbazole had a greatly lowered m. p.

9-p-*Bromophenylcarbazole* gave a **2 : 4 : 7-*trinitrofluorenone complex*** (from acetic acid) in plates which were scarlet by transmitted, but purple-black by reflected, light, m. p. 168—170° (Found: C, 58·2; H, 2·9; N, 8·8. $C_{18}H_{12}NBr,C_{13}H_5O_7N_3$ requires C, 58·4; H, 2·7; N, 8·8%).

We are extremely grateful to Professor Melvin S. Newman for a gift of (−)-α-(2 : 4 : 5 : 7-tetranitro-9-fluorenylideneamino-oxy)propionic acid. We also thank Mr. J. M. L. Cameron and Miss S. U. Watt for the microanalyses.

THE UNIVERSITY, GLASGOW. [*Received, February 13th*, 1958.]

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562. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part VII.* Some Experiments relating to the Halogenation of Toluene and* tert.*-Butylbenzene.*

By P. B. D. de la Mare, J. T. Harvey, M. Hassan, and S. Varma.

The acid-catalysed chlorination of toluene by hypochlorous acid in water is 60 times faster than that of benzene, and gives *o*- 74·6%, *m*- 2·2%, and *p*-chlorotoluene 23·2%. Chlorination of *tert.*-butylbenzene by molecular chlorine in 99% acetic acid is accompanied by 0·13% of chlorodebutylation. The proportion of *meta*-substitution in the bromination of toluene by molecular bromine in 87·5% acetic acid, as determined by the method of isotopic dilution, is 0·20%. With hypochlorous acid in 75% acetic acid, *tert.*-butylbenzene gives 42% of *p-tert.*-butylchlorobenzene. Comparison with results for other electrophilic reagents indicates that there is appreciable steric hindrance to the *ortho*-chlorination of *tert.*-butylbenzene by positive chlorine, and suggests that there may be a little steric hindrance to the *ortho*-bromination of toluene by positive bromine.

Bromination of toluene, by acidified hypobromous acid as the source of bromine, gives 70·3% of *ortho*-substitution.[1] Molecular bromine, on the other hand, gives predominantly *para*-substitution.[2,3] It is of interest to see whether a difference of this kind applies also to chlorination, and therefore the partial rate factors have been determined for the acid-catalysed chlorination of toluene in water. We had intended to extend this work to a study of the chlorination by molecular chlorine of toluene and *tert.*-butylbenzene; but data on these topics have now been presented by H. C. Brown and his co-workers[3,4] so herein are presented only such of our results as usefully extend their measurements.

Experimental

Most of the materials and general methods have been described in previous papers.[1,2,5] The chlorotoluenes were commercial specimens, carefully purified by fractional distillation, and had b. p. at 760 mm.: *o*-, 159°; *m*-, 161°; *p*-, 162°. *p-tert.*-Butylchlorobenzene, prepared from *p-tert.*-butylaniline by the Sandmeyer method and purified by fractional distillation and fractional freezing, had m. p. 23·7°. Other samples were prepared by fractional crystallisation from ethanol of specimens prepared by chlorination of *tert.*-butylbenzene.

Kinetics of Chlorination in Water.—The measurements were made in the presence of 0·01M-silver perchlorate, to repress the formation of free chlorine. Controls showed that the decomposition of hypochlorous acid could be neglected. The following example is typical of the rate-measurements all of which were made at 25°. From a solution containing 0·0088M-toluene, 0·0004M-hypochlorous acid, 0·01M-silver perchlorate, and 0·60M-perchloric acid, samples (25 ml.) were removed at intervals for titration with sodium thiosulphate. Results were:

Time (min.)	0·0	10·0	20·0	30·0	40·0	50·0	60·0	75·0
Titre (ml. of 0·004-N-$Na_2S_2O_3$)	5·00	4·55	4·15	3·80	3·50	3·25	3·00	2·50
k_2 (l. mole^{-1} min.$^{-1}$)	—	1·1	1·0	1·0	1·0	1·0	0·9	1·0

The following are mean values of k_2 (l. mole^{-1} min.$^{-1}$) for substantially similar concentrations of toluene, hypochlorous acid, and silver perchlorate at various acidities:

$HClO_4$ (M)	0·184	0·60	1·00	1·20	1·38
k_2 (l. mole^{-1} min.$^{-1}$)	0·28	1·0	1·4	1·8	2·5
k_2/H^+ (l.^{2} mole^{-2} min.$^{-1}$)	1·5	1·7	1·4	1·5	1·8

* Part VI, *J.*, 1958, 1519.

[1] de la Mare and Harvey, *J.*, 1956, 36.
[2] Robertson, de la Mare, and Swedlund, *J.*, 1953, 782.
[3] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 1421.
[4] *Idem*, *ibid.*, p. 5175.
[5] de la Mare, Ketley, and Vernon, *J.*, 1954, 1290.

Corresponding values for benzene (0·22—0·37M) with hypochlorous acid (*ca.* 0·004M) are as follows (values of h_0 have been taken from Paul and Long's review [6]):

$HClO_4$ (M)	1·00	2·00	2·30	3·00	4·00	5·00
k_2 (l. mole^{-1} min.$^{-1}$)	0·025	0·11	0·18	0·60	1·8	3·9
k_2/H^+ (l.^{2} mole^{-2} min.$^{-1}$)	0·025	0·056	0·078	0·20	0·45	0·78
k_2/h_0 (l.^{2} mole^{-2} min.$^{-1}$)	0·015	0·018	0·023	0·035	0·034	0·023

Isomeric Proportions in the Chlorination of Toluene in Water.—The method of isotopic dilution was used. The tracer was introduced into the reaction mixture as hypochlorous acid, (HO^{36}Cl), and the mixed products were diluted with the appropriate inactive chlorotoluene. Final estimates of radioactivity were made after oxidation to the corresponding benzoic acid. Allowance was made for decomposition of hypochlorous acid by means of a control experiment. For the determination of *m*-chlorotoluene, the final measurement of radioactivity was made after adding, to the nearly pure *m*-chlorobenzoic acid, inactive *o*- and *p*-chlorobenzoic acid to act as hold-back carriers. The product was then again recrystallised until the m. p. was 157—158°, and the specific activity was unchanged on further recrystallisation. A solution (0·17M), in alkali, of the finally recovered acid had, after correction for background, an activity of 39 counts/min., quite high enough for satisfactory measurement. The values obtained were: *o*-, 74·4; *m*-, 2·2; and *p*-, 23·1%; the total (99·7%) accounts for all the reaction within experimental error.

Chlorodebutylation of tert.-*Butylbenzene in* 99% *Acetic Acid.*—*tert.*-Butylbenzene (0·1157M) and $^{36}Cl_2$ (0·0840M) were allowed to react to completion. To the product, which should have contained 2·803 g. of mixed *tert.*-butylchlorobenzenes, was added inactive chlorobenzene (11·99 g.). This was recovered by fractional distillation and nitrated. The resulting 1-chloro-2 : 4-dinitrobenzene was recrystallised till its activity was 26 counts/min. (1·0M). The chlorine solution converted into lithium chloride had an activity of 120 counts/min. (0·00092M). Hence not more than 0·13% of chlorobenzene was produced in the reaction by chlorodebutylation. To the residue of highly active *tert.*-butylchlorobenzenes was added more chlorobenzene, and the mixture was fractionated as before. The recovered chlorobenzene had negligible activity.

p-*Chlorination of* tert.-*Butylbenzene by Hypochlorous Acid in* 75% *Acetic Acid.*—The method of isotopic dilution was used, final measurements of radioactivity being made on *p-tert.*-butylchlorobenzene. There was formed 42% of *p-tert.*-butylchlorobenzene.

m-*Bromination of Toluene by Molecular Bromine in* 87·5% *Acetic Acid.*—Toluene (0·130M) and bromine (0·130M) in 87·5% acetic acid were allowed to react until 1·06 g. of bromotoluenes had been produced in 480 ml. of solution. Then were added sodium formate and 11·07 g. of inactive *m*-bromotoluene. The mixed bromotoluenes were recovered and oxidised; recrystallisation of the acidic product gave *m*-bromobenzoic acid (2 g.; m. p. 155°). This was further recrystallised to constant specific activity; treatment with *o*- and *p*-bromobenzoic acid as hold-back carriers did not further reduce the specific activity. The original hypobromous acid had an activity of 470 counts/min. (0·000445M). The diluted pure *m*-bromobenzoic acid had an activity, at the same time, of 62·3 counts/min. (0·302M). Hence 0·00217 g. (0·20%) of *m*-bromotoluene was produced in the reaction. This value is slightly smaller than those (0·24, 0·30%) obtained by Brown and Stock,[3] using the method of infrared analysis, for reaction in a slightly more aqueous solvent. The method of isotopic dilution, when applied to components present in such small proportions, is more likely to give high than low values, so it is considered that the present figure reliably estimates the amount of *m*-bromination under the conditions adopted.

Discussion

Chlorodebutylation by Molecular Chlorine.—In Part III [7] it was shown that, for the reaction of *tert.*-butylbenzene with acidified hypobromous acid, bromodebutylation contributed to the reaction to the extent of about 1·9 moles %, the partial rate factor for this reaction being rather greater than that for attack by this reagent on a single position in benzene itself. For chlorination by molecular chlorine, proportionately less debutylation accompanies the reaction. Using the relative reactivities of benzene and *tert.*-butylbenzene recorded elsewhere [8] leads to a partial rate factor for chlorodebutylation of about

[6] Paul and Long, *Chem. Rev.*, 1957, **87**, 1.
[7] de la Mare and Harvey, *J.*, 1957, 131.
[8] de la Mare and Robertson, *J.*, 1943, 279.

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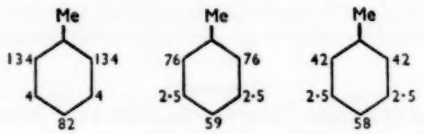
1; so the smaller proportion is mainly a reflection of the greater spread of reactivities conferred by substituents in chlorination by molecular chlorine than in bromination by positive bromine.

Chlorination of Toluene in Water.—The chlorination of toluene and of benzene by hypochlorous acid in water followed the kinetic form, $-d[ClOH]/dt = k[ArH][ClOH]f(H^+)$. In the region of acidity below about 1M-perchloric acid, the rate of reaction depends directly on the concentration of acid, and the rate-comparison used below represents an estimate, from the graphs of rate against concentration of acid, of the relative rates of reaction at 1·0M-perchloric acid.

With higher concentrations of acid, the rate increases more rapidly, being approximately proportional, up to 5M-perchloric acid, to the value of Hammett's acidity function, h_0. This proportionality is shown by the ratios, given above, of k_1/h_0; such behaviour accords, as far as can be seen from their graphs, with that recorded by Derbyshire and Waters [9] for the acid-catalysed chlorination of sodium toluene-ω-sulphonate by hypochlorous acid. It is a result which is not unexpected for a reaction involving a pre-equilibrium proton-transfer, $ClOH + H^+ \rightleftharpoons ClOH_2^+$. The data are not such as to allow a test of the hypothesis [10] that the rate might follow the acidity function J_0, if, as would be required by the theory discussed elsewhere,[5] the above pre-equilibrium were followed by the formation of Cl^+ by the equilibrium: $ClOH_2^+ \rightleftharpoons Cl^+ + H_2O$. It seems probable that J_0 does not differ very considerably from H_0 in the experimental region under consideration.

The rate of reaction of sodium toluene-ω-sulphonate is, at any given acidity, one-third of that of benzene, the former reaction having been investigated at 21·5° and the latter at 25°. The kinetic form for the former reaction shows that it is a reaction of the negative ion, $Ph{\cdot}CH_2{\cdot}SO_3^-$; and the $\cdot CH_2{\cdot}SO_3^-$ grouping in this compound is known to be substantially *ortho-para*-directing, both for nitration [11] and for chlorination in water.[12] If, as in nitration, chlorination gives about 50% of the *para*-isomer, then, when allowance is made for the slightly lower temperature used in Derbyshire and Waters's measurements, the *para*-position in the toluene-ω-sulphonate ion can be estimated to be slightly activated relative to a single position in benzene, and of course deactivated relative to the *para*-position in toluene. The negative charge on the SO_3^- group is not, apparently, sufficient to overcome the electron-withdrawing inductive effect of the powerfully electronegative sulphur atom formally one atom nearer to the aromatic ring.

The experimentally determined proportions of isomers in the chlorination of toluene account for 99·7% (*i.e.*, all, within experimental error) of the uptake of hypochlorous acid; the normalised figures used in the calculation of partial rate factors are: *o*, 74·6; *m*, 2·2; *p*, 23·2%. These, and the relative rates of reaction of toluene and benzene in 1M-perchloric acid (60 : 1, from the graphs of rate against acidity) give the partial rate factors shown in the diagram and there compared with those for other aromatic replacements by positively charged reagents in hydroxylic solvents.[1,13]



Cl^+ Br^+ (or $BrOH_2^+$) NO_2^+

The $\frac{1}{2}m : p$-ratios in the three reactions (0·049, 0·042, and 0·042) are approximately constant. It seems reasonable, therefore, to attribute the corresponding decrease in

[9] Derbyshire and Waters, *J.*, 1951, **73**.
[10] Gold and Hawes, *J.*, 1951, 2102.
[11] Ingold, Ingold, and Shaw, *J.*, 1927, 828.
[12] D.R.-P. 146,946; cf. *Chem. Zentr.*, 1904, **75**, I, 66.
[13] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291.

$\frac{1}{2}o$: *p*-ratio (1·64, 1·28, 0·73) to increase in steric inhibition by the *o*-methyl group, in the order $Cl^+ < Br^+ < NO_2^+$, for introduction of these groups by a positively charged electrophilic entity. The order $Cl_2 < Br_2$ is well established for molecular halogenation, and is generally attributed to steric effects.[3,4,14]

This view receives some support when the proportions of *para*-substitution in toluene and *tert.*-butylbenzene are compared. Limitations of solubility have prevented us from examining *tert.*-butylbenzene in water; but it can be chlorinated with hypochlorous acid in aqueous acetic acid, in which solvent the reagent is a positive species.[15] The annexed

Percentage of para-*substitution in some alkylbenzenes.*

Reagent	Solvent	% *para*-Substitution Toluene	*tert.*-Butylbenzene	Ref.
Positive chlorine ...	H_2O	23	42 (solvent aq. HOAc)	This paper
Positive bromine ...	H_2O	27·4	53·2	1, 7
NO_2^+	aq. HOAc	40·0	79·5	13
Cl_2	HOAc	40	76	4, and H. C. Brown and L. M. Stock, personal communication
Br_2	aq. HOAc	67	92	1, 2, 3

Table shows the percentage of *para*-substitution under various conditions. Qualitatively, substitution is always relatively less easy *ortho* to a *tert.*-butyl group; this has, for the other reagents,[1,3,13] been attributed to steric hindrance, so it seems reasonable to use the same explanation for chlorination of *tert.*-butylbenzene by positive chlorine, and to believe that there may be a small residue of differential steric hindrance manifest in the comparison of bromination and chlorination of toluene by positive reagents.

The authors are indebted to Professor Sir Christopher Ingold, F.R.S., and to Professor E. D. Hughes, F.R.S., for their continued interest and for comments on this manuscript.

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[14] Holleman, *Chem. Rev.*, 1925, **1**, 187.
[15] de la Mare, Ketley, and Vernon, *Research*, 1953, **6**, 12s.

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563. *Stereochemical Investigations of Cyclic Bases. Part III.* An Example of Wagner–Meerwein Elimination with a Quaternary Ammonium Salt.*

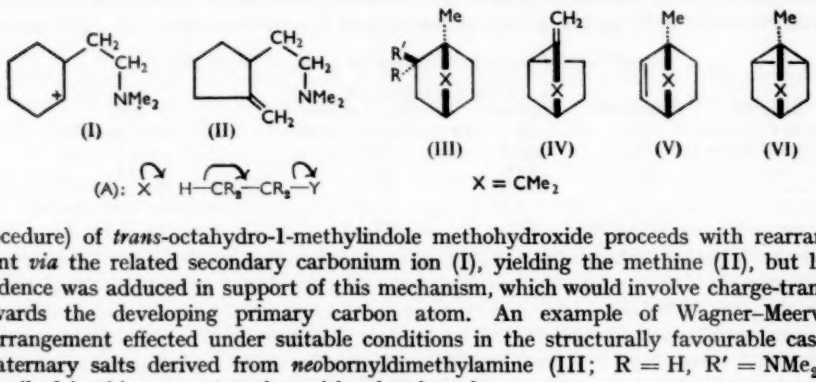
By J. MCKENNA and J. B. SLINGER.

Pyrolysis of dry bornyltrimethylammonium hydroxide yields pure bornylene, and this hydrocarbon is also the chief decomposition product of *neo*bornyltrimethylammonium hydroxide or of the corresponding epimeric amine oxides. Nearly pure camphene is obtained by heating neutral or alkaline aqueous or glycol solutions of *neo*bornyltrimethylammonium iodide: the rate of hydrocarbon formation is independent of alkali concentration, but camphene of high optical purity is obtained only from the alkaline degradations. Hot alkaline solutions of bornyltrimethylammonium iodide yield only the tertiary base by methanol elimination, a reaction which also proceeds more slowly with the epimeric salt.

BOTH *E*1 and *E*2 mechanisms have been established kinetically for a wide range of variables X and Y in the elimination reaction involving the process (A). However, Hofmann elimination of quaternary ammonium salts ($Y = Alk_3N^+$) usually proceeds by the *E*2 process, although there are[1] a few examples † where the alternative mechanism seems

* Part II, *J.*, 1958, 2209.
† We thank a referee for drawing our attention to these examples.
[1] Norcross and Openshaw, *J.*, 1949, 1174; Pailer and Bilek, *Monatsh.*, 1948, **79**, 135.

probable, although it has not been fully established. Ease of unimolecular elimination is enormously increased if a combination of polar and stereoelectronic factors facilitates rearrangement of the developing carbonium ion, but we are unaware of any previous adequate demonstration (*i.e.*, structural and kinetic) of Wagner–Meerwein rearrangement during a Hofmann elimination reaction of a quaternary ammonium salt. King and Booth have suggested [2] however, that thermal degradation (by the conventional experimental



procedure) of *trans*-octahydro-1-methylindole methohydroxide proceeds with rearrangement *via* the related secondary carbonium ion (I), yielding the methine (II), but little evidence was adduced in support of this mechanism, which would involve charge-transfer towards the developing primary carbon atom. An example of Wagner–Meerwein rearrangement effected under suitable conditions in the structurally favourable case of quaternary salts derived from *neo*bornyldimethylamine (III; R = H, R′ = NMe_2) is described in this paper, together with related work.

The preparation and characterisation, from (+)-camphor,‡ of (+)-bornylamine (III; R = NH_2, R′ = H), (−)-*neo*bornylamine (III; R = H, R′ = NH_2) and their *NN*-dimethyl derivatives is described in the Experimental section; three of these bases have been prepared before, but our work includes improvements in preparative methods and some correction and extension of data in previous literature. Of some theoretical interest is the isolation of camphor during formaldehyde–formic acid methylation of either primary amine: as this result suggests the equilibrium of intermediates $>CH{\cdot}N{:}CH_2 \rightleftharpoons >C{:}N{\cdot}CH_3$, formation of some epimeric tertiary base might be expected, but our work indicates that (as in some related examples in the literature [3,4]) no appreciable epimerisation does in fact occur. *cyclo*Pentylamine and *cyclo*hexylamine gave much lower yields of ketone during methylation, with no significant [5] preferential formation of *cyclo*pentanone.

Ionic eliminations with 2-substituted camphanes usually yield mainly camphene (IV) together with varying proportions of bornylene (V) and tricyclene (VI). When conditions strongly favour *E*2 elimination the chief product is bornylene, which can be obtained, for example,[6] with 93% purity (7% of camphene) from bornyl halides and potassium pentyloxide in dry pentanol at 190—230°. However, Ruzicka's thermal degradation [7] of what was evidently a mixture of bornyl- and *neo*bornyl-trimethylammonium hydroxides has been the only elimination process previously claimed to yield pure bornylene directly from a 2-substituted camphane, although Shriner and Sutherland have stated,[8] without experimental evidence, that the olefinic product contains *ca.* 4% of camphene. Neither

‡ For the absolute configuration of (+)-camphor and related compounds see Birch, *Ann. Reports*, 1950, **47**, 191, and Prelog and Meier, *Helv. Chim. Acta*, 1953, **36**, 320. All active terpenes described in this paper are configurationally related to (+)-camphor.

[2] King and Booth, *J.*, 1954, 3798.
[3] Parham, Hunter, Hanson, and Lahr, *J. Amer. Chem. Soc.*, 1953, **74**, 5646; Grob, Kny, and Gagneux, *Helv. Chim. Acta*, 1957, **40**, 130.
[4] Cope and Bumgardner, *J. Amer. Chem. Soc.*, 1957, **79**, 960.
[5] Cf. Brown, *J. Org. Chem.*, 1957, **22**, 439.
[6] Meerwein and Joussen, *Ber.*, 1922, **55**, 2529.
[7] Ruzicka, *Helv. Chim. Acta*, 1920, **3**, 748.
[8] Shriner and Sutherland, *J. Amer. Chem. Soc.*, 1938, **60**, 1314.

Shriner and Sutherland nor Ruzicka investigated the degradation of both individual epimeric quaternary salts, or the effect of changing the reaction conditions.

When dry bornyl- or *neo*bornyl-trimethylammonium hydroxide or a mixture of the two was heated at temperatures up to 180°, the quaternary bases remained solid, and bornylene slowly distilled together with some tertiary amine. Experiments in which mixtures of the epimeric quaternary hydroxides were pyrolysed indicated that bornyltrimethylammonium hydroxide decomposed more slowly than its epimer, but gave a higher proportion of the related tertiary amine. Ruzicka also obtained a tertiary base by pyrolysis of a mixture of the quaternary hydroxides; he characterised the base by conversion into the methiodide, which was incorrectly regarded, however, as being mainly the *neo*(or *iso*)-epimer. The bornylene obtained by pyrolysis of dry bornyltrimethylammonium hydroxide appeared to be quite pure, but the *neo*-hydroxide yielded a hydrocarbon containing some tricyclene. Bornyltrimethylammonium hydroxide when not quite dry was molten at 180°, and at that temperature yielded a hydrocarbon containing a trace of camphene; this may explain the slight discrepancy between the results of Ruzicka and of Shriner and Sutherland. In spite of the great ease of rearrangement of the camphane carbon framework, it is evident that the Wagner–Meerwein elimination cannot compete effectively with the normal $E2$ and S_N2 reactions in the extremely strongly basic conditions obtaining when the Hofmann degradation is carried out in the conventional manner [9] (*i.e.*, evaporation of aqueous quaternary hydroxide,* followed by pyrolysis), and it appeared desirable to study the elimination at moderate dilutions in ionising solvents.

Distillation of an alkaline solution of (−)-*neo*bornyltrimethylammonium iodide in aqueous glycol yielded some tertiary base and (+)-camphene; the latter, although containing traces of bornylene and tricyclene, was of higher optical purity than was obtainable by any other elimination process from a 2-substituted camphane, either directly or even after further purification. Similar treatment of bornyltrimethylammonium iodide yielded no hydrocarbon, but only tertiary base. Complete alkaline decomposition of approximately equimolar mixtures of the epimeric methiodides gave camphene, and, in the basic fraction, mainly bornyldimethylamine; nearly pure samples of this tertiary base were obtained from mixed methiodide degradations in glycol which was only weakly alkaline. These results are chiefly due to the much more rapid conversion of the *neo*-salt into hydrocarbon; the rate of this reaction in glycol, as in water, is probably alkali-independent (see below) while the rates of the competitive methanol-elimination reactions are probably alkali-dependent (S_N2). Camphene was also obtained by dry pyrolysis of *neo*bornyltrimethylammonium iodide at 180°; at this temperature the epimeric salt was stable, but at 250° it gave bornyldimethylamine and a neutral oil containing some camphene.

Experiments in which methiodide mixtures were partly (*ca.* 20%) decomposed in alkaline solution showed that the methanol-elimination (reversion to tertiary base) with the bornyl quaternary salt (less hindered N) was slightly faster than with the epimer. This rather unexpected result indicates that relief of strain at the quaternary nitrogen atoms during formation of the transition state is not the controlling factor in determining the relative rates of the methanol-elimination with this particular pair of quaternary salts. Bornyl and *neo*bornyl epimers, however, do not differ considerably in degree of steric compression at the functional groups.

That the conversion of (−)-*neo*bornyltrimethylammonium iodide into (+)-camphene is a conventional (carbonium ion) Wagner–Meerwein rearrangement was demonstrated by experiments in aqueous solution at 140°: the rate of formation of hydrocarbon was independent of hydroxide-ion concentration. The camphene from neutral degradations was found to be partly racemised, and was significantly (no $E2$ reaction) free from bornylene.

* We did this *in vacuo* at room temperature for manipulative convenience, but solutions of the quaternary hydroxide decompose only very slowly at 100° (see Experimental section).

[9] Cf. Weinstock, *J. Org. Chem.*, 1956, **21**, 540.

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Racemisation appears to occur during, and not after, formation of hydrocarbon, and is possibly related to the longer life in neutral solution of the related carbonium ion, which is an intermediate in either of the two possible racemisation mechanisms.[10] Elimination of methanol from *neo*bornyltrimethylammonium hydroxide was not observed even in strong aqueous alkali; the reaction is more readily suppressed in water than in glycol, probably because water is such a favourable solvent for the competitive rearrangement.

Degradation of alicyclic amine oxides to olefins and alkylhydroxylamines assumes a *cis*-steric course,[11] and we have found that pyrolysis of the *N*-oxides of (+)-bornyl- and (−)-*neo*bornyl-dimethylamine affords hydrocarbon mixtures similar to those obtained from the mechanistically related pyrolysis of the xanthate esters of borneol and *neo*-borneol, which yield [12] respectively bornylene contaminated with a little tricyclene, and a mixture of equal parts of bornylene and camphene; not so much camphene, however, is formed on pyrolysis of *neo*bornyldimethylamine oxide. These pyrolyses also yielded some tertiary base, less with the *neo*bornyl than with the bornyl epimer.

By a combination of reactions described in this paper samples of nearly pure optically active camphene and quite pure active bornylene may rapidly and conveniently be prepared from the active camphor of related configuration. This is converted into a mixture of epimeric trimethylammonium iodides, which on distillation with alkaline glycol yields camphene and mainly bornyldimethylamine; this base is then converted into quaternary hydroxide, dry distillation of which gives bornylene.

Experimental

Except where stated otherwise, optical rotations refer to EtOH solutions at room temperature (17—23°) at concentrations of 0·5—2% (usually nearer the higher value) in 2 dm. tubes of internal diameter 6 mm.

(+)-*Bornylamine*.—Reduction of (−)-camphor oxime with sodium in pentanol gave a mixture containing (optical rotation) (+)-bornylamine (70%) and (−)-*neo*bornylamine (30%). Several successive recrystallisations of this mixture from dilute hydrochloric acid gave (+)-bornylamine hydrochloride, m. p. 330°, $[\alpha]_D$ +23° (Found: C, 63·3; H, 10·5; N, 7·4; Cl, 18·9. Calc. for $C_{10}H_{20}NCl$: C, 63·3; H, 10·6; N, 7·4; Cl, 18·7%). The base had m. p. 159°, $[\alpha]_D$ +46° (Found: C, 78·4; H, 12·5; N, 9·1. Calc. for $C_{10}H_{19}N$: C, 78·3; H, 12·4; N, 9·2%). The *N*-benzoyl derivative, m. p. 138°, $[\alpha]_D$ −23° (Found: C, 79·2; H, 9·0; N, 5·5. Calc. for $C_{17}H_{23}ON$: C, 79·3; H, 9·0; N, 5·5%), picrate, m. p. 245—247° (decomp.) (Found: C, 50·3; H, 5·9; N, 14·5. Calc. for $C_{16}H_{22}O_7N_4$: C, 50·3; H, 5·8; N, 14·7%), and *picrolonate*, needles (from ethanol), m. p. 260° (decomp.) (Found: C, 57·6; H, 6·6; N, 16·7. $C_{20}H_{27}O_5N_5$ requires C, 57·5; H, 6·5; N, 16·8%), were prepared. The physical constants for previously known compounds agree with those quoted in the literature.[13]

(+)-*Bornyldimethylamine and* (−)-*Bornyltrimethylammonium Iodide from* (+)-*Bornylamine*.—(a) *Formaldehyde–formic acid method*. A mixture of (+)-bornylamine (820 mg.), 40% aqueous formaldehyde (2·5 c.c.), and 98% formic acid (6 c.c.) was heated under reflux for 12 hr. on the steam-bath, and the products were separated into (+)-camphor (138 mg.), m. p. and mixed m. p. 174°, $[\alpha]_D$ +50° (in Et_2O) [dinitrophenylhydrazone, m. p. and mixed m. p. 174·5° (Found: C, 57·8; H, 6·0; N, 16·9. Calc. for $C_{16}H_{20}O_4N_4$: C, 57·8; H, 6·0; N, 16·9%)], and (+)-*bornyldimethylamine* (800 mg.), b. p. 216°/744 mm., $[\alpha]_D$ +27°, increased to +34° on purification by the countercurrent process described below (p. 2764), n_D^{26} 1·4772 (Found: C, 79·7; H, 12·8; N, 7·6. $C_{12}H_{23}N$ requires C, 79·5; H, 12·8; N, 7·7%). Forster [14] records b. p. 210—212°/763 mm., $[\alpha]_D$ +48·7° (in EtOH), but this value of $[\alpha]$ is criticised by later workers [15] who give $[\alpha]_D$ +34·86° (but no analysis) for the liquid base. The *hydrochloride* was obtained

[10] Roberts and Yancey, *J. Amer. Chem. Soc.*, 1953, **75**, 3165.
[11] *Inter al.*, Cope, Pike, and Spencer, *ibid.*, p. 3212, and other papers by Cope and his collaborators.
[12] Tschugaeff and Budrich, *Annalen*, 1912, **388**, 280; Henderson and Caw, *J.*, 1912, **101**, 1416; Shavrygin, *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 807 (*Chem. Abs.*, 1941, **35**, 2491).
[13] Josephy and Radt (Ed.), "Encyclopaedia of Organic Chemistry," Elsevier, Amsterdam, 1948, Vol. 12A, pp. 609—611.
[14] Forster, *J.*, 1899, **75**, 934.
[15] Ives and Nettleton, *J.*, 1948, 1085.

as needles (from chloroform–ether), m. p. 220°, $[\alpha]_D$ +9° (Found: N, 6·4. $C_{13}H_{24}NCl$ requires N, 6·4%): Forster [14] records m. p. >300°, $[\alpha]_D$ +37·2° (in EtOH). The *picrate*, yellow rods (from ethanol), had m. p. 213—214°, not depressed on admixture with the salt from preparations (b) and (c) (Found: C, 52·8; H, 6·5; N, 13·6. $C_{16}H_{24}O_7N_4$ requires C, 52·7; H, 6·4; N, 13·7%). With methyl iodide in boiling methanol the tertiary base prepared by method (a) was converted into (−)-bornyltrimethylammonium iodide, leaflets, m. p. (from ether–methanol) 276°, after discoloration at 270°, $[\alpha]_D$ −3·6° (Found: C, 48·3; H, 8·1; N, 4·1; I, 39·1. Calc. for $C_{13}H_{26}NI$: C, 48·3; H, 8·1; N, 4·2; I, 39·3%). Forster,[14] who prepared the methiodide from (+)-bornylamine with methyl iodide and alcoholic sodium hydroxide, records m. p. >250°, $[\alpha]_D$ −3·9° (in EtOH).

(b) Via N-*methylbornylamine*. (+)-Bornylamine (1·37 g.) was treated with 98% formic acid (5 c.c.) at 100° for 12 hr., neutral and basic products were separated, and the base was again treated with formic acid. The crude *N*-formyl derivative (1·12 g.) in boiling ether (500 c.c.) was reduced with lithium aluminium hydride (0·6 g.) for 4 hr. The secondary amine was isolated as the *hydrochloride* (1·2 g.) which formed rectangular plates, m. p. >300°, $[\alpha]_D$ +38°, after crystallisation from ethanol (Found: C, 64·6; H, 11·0; N, 6·8; Cl, 17·3. $C_{11}H_{22}NCl$ requires C, 64·8; H, 10·9; N, 6·9; Cl, 17·4%). Forster [14] records m. p. >250°, $[\alpha]_D$ +31° (in EtOH), and gives no analysis. The *N*-benzoyl derivative had m. p. 126° (lit.,[14] 127°) (Found: C, 79·4; H, 9·2; N, 5·3. Calc. for $C_{18}H_{25}ON$: C, 79·7; H, 9·2; N, 5·2%). Methylation of the secondary base with formaldehyde and formic acid yielded no camphor; the (+)-bornyldimethylamine was characterised as the hydrochloride, $[\alpha]_D$ +7·7°, and the picrate, m. p. 209—210°.

(c) *By methylation with methyl iodide*. A mixture of (+)-bornylamine hydrochloride (7·8 g.), potassium carbonate (6 g.), methyl iodide (25 c.c.), and acetone (750 c.c.) was refluxed overnight, and the quaternary salt isolated in chloroform; it had m. p. 276° (decomp. at 270°) and $[\alpha]_D$ −3·7° (Found: C, 48·1; H, 8·1; N, 4·2; I, 39·6. Calc. for $C_{13}H_{26}NI$: C, 48·3; H, 8·1; N, 4·2; I, 39·3%). The *X*-ray powder photograph and infrared absorption spectrum of this methiodide were identical with those obtained with the salt prepared by method (a). Reduction of the methiodide (1·48 g.) by refluxing it in tetrahydrofuran (125 c.c.) with lithium aluminium hydride [4] (1·8 g.) for 84 hr. gave (+)-bornyldimethylamine (740 mg.), n_D^{25} 1·4775 (Found: C, 79·6; H, 12·7; N, 8·0. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%), from which the hydrochloride, $[\alpha]_D$ +7·1°, and the picrate, m. p. and mixed m. p. 213—214°, were prepared.

(−)-neo*Bornylamine*.—This amine was obtained as hydrochloride by application of Goodson's technique [16] (distribution between ether and dilute hydrochloric acid in separating funnels) to the residual hydrochlorides from the oxime reduction (after crystallisation of bornylamine hydrochloride) or to a mixture of (−)-*neo*bornylamine hydrochloride (65%) and (+)-bornylamine hydrochloride (35%) derived from (+)-camphor by the Leuckart reaction. The *neo*-epimer (weaker base [17]) was preferentially extracted by the ether. The oxime reduction residues also appeared to contain some dibornylamine or an isomer. (−)-*neo*-Bornylamine hydrochloride after recrystallisation from chloroform–ether had m. p. 324° and $[\alpha]_D$ −48° (Found: C, 63·1; H, 10·4; N, 7·4; Cl, 18·5. Calc. for $C_{10}H_{20}NCl$: C, 63·3; H, 10·6; N, 7·4; Cl, 18·7%). Goodson [16] gives $[\alpha]_D$ −49°.

(−)-neo*Bornyldimethylamine and* (−)-neo*Bornyltrimethylammonium Iodide*.—(*a*) Methylation of (−)-*neo*bornylamine (590 mg.) with 40% aqueous formaldehyde (1·95 c.c.) and 98% formic acid (4·7 c.c.) at 100° overnight gave camphor (100 mg.), m. p. 172° (dinitrophenylhydrazone, m. p. and mixed m. p. 174°), and (−)-*neo*bornyldimethylamine (510 mg.) from which the hydrochloride, $[\alpha]_D$ −60°, and the picrate, m. p. 194°, were prepared, identical with the compounds prepared by methods (*b*) and (*c*).

(*b*) A mixture of (−)-*neo*bornylamine hydrochloride (260 mg.), potassium carbonate (5 g.), methyl iodide (5 c.c.), and acetone (60 c.c.) was refluxed overnight. The resulting (−)-neo-*bornyltrimethylammonium iodide* (204 mg.) separated from ether–methanol in rods, m. p. 242° (with some preliminary decomp.), $[\alpha]_D$ −34° (Found: C, 48·4; H, 8·2; N, 4·2; I, 39·1. $C_{13}H_{26}NI$ requires C, 48·3; H, 8·1; N, 4·3; I, 39·3%). Reduction of this methiodide with lithium aluminium hydride in tetrahydrofuran by the method described for the epimeric salt yielded (−)-*neo*bornyldimethylamine which gave the hydrochloride, $[\alpha]_D$ −64°, and the picrate, m. p. 194°.

[16] Goodson, *J.*, 1927, 930.
[17] Girault-Vexlearschi, *Bull. Soc. chim. France*, 1956, 589.

(*c*) A mixture of *N*-formylbornylamine and *N*-formyl*neo*bornylamine derived from a Leuckart reaction with (+)-camphor (7 g.) was reduced in ether (500 c.c.) with lithium aluminium hydride (2 g.) for 12 hr. and the resulting mixture of secondary amines (5·8 g.) converted into mixed tertiary bases (6·0 g.), $[\alpha]_D$ −30° (Found: C, 79·8; H, 12·8; N, 7·7. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%), with formaldehyde and formic acid. Separation of the tertiary bases was most readily achieved by countercurrent distribution in a Craig apparatus between ether and a phosphate buffer (pH 6·6), the *neo*-base again being preferentially extracted by the ether. This process yielded (+)-bornyldimethylamine, $[\alpha]_D$ +34° (hydrochloride, $[\alpha]_D$ +9°), and (−)-neo*bornyldimethylamine*, b. p. 210°/744 mm., n_D^{25} 1·4792, $[\alpha]_D$ −61° (Found: C, 79·5; H, 12·4. $C_{12}H_{23}N$ requires C, 79·5; H, 12·8%) which gave a *hydrochloride*, needles from (chloroform–ether), m. p. 243°, $[\alpha]_D$ −63° (Found: C, 66·1; H, 10·5; N, 6·8. $C_{12}H_{24}NCl$ requires C, 66·2; H, 11·1; N, 6·4%), and a *picrate*, rods (from ethanol), m. p. 194° (Found: C, 52·5; H, 6·2; N, 13·4. $C_{18}H_{26}O_7N_4$ requires C, 52·7; H, 6·4; N, 13·7%). The methiodide from the tertiary base was identical with that obtained directly from (−)-*neo*bornylamine by method (*b*), having m. p. 242° (preliminary decomp.) and $[\alpha]_D$ −33° (Found: C, 48·5; H, 8·0; N, 4·2; I, 39·7. Calc. for $C_{13}H_{26}NI$: C, 48·3; H, 8·1; N, 4·3; I, 39·3%).

Methylation of cyclo*Hexyl- and* cyclo*Pentyl-amine.*—After gradual heating (exothermic reaction), a mixture of *cyclo*hexylamine (25 g.), 98% formic acid (45 c.c.), and 40% aqueous formaldehyde (40 c.c.) was kept at 100° for 1 hr. Dilution with water and extraction with light petroleum (b. p. 40—60°) yielded a neutral oil (262 mg.) which yielded *cyclo*hexanone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 158° (Found: C, 51·3; H, 5·5; N, 20·1. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·1; N, 20·1%). *cyclo*Hexyldimethylamine (19·2 g.), b. p. 158°, was obtained from the acid solution.

From *cyclo*pentylamine (16·2 g.) were likewise obtained crude *cyclo*pentanone (376 mg.) [2 : 4-dinitrophenylhydrazone, m. p. 140°; lit., 146°] and *cyclo*pentyldimethylamine (9·0 g.), b. p. 131°, which yielded the picrate,[18] m. p. 176—177° (Found: C, 45·5; H, 5·2; N, 16·4. Calc. for $C_{13}H_{18}O_7N_4$: C, 45·6; H, 5·3; N, 16·4%). Some basic resinous by-products were formed during each methylation.

Infrared Spectra of Camphene, Tricyclene, and Bornylene.—The infrared spectra of these hydrocarbons and of mixtures from the elimination reactions were observed usually in Nujol mulls or occasionally in carbon disulphide, band positions under either conditions being almost the same. Our curves for camphene and tricyclene covered a slightly different range, but otherwise agreed closely with those of Swann and Cripwell,[19] showing bands in Nujol at (for camphene), 670, 747, 760, 810, and 877 cm.$^{-1}$ and (for tricyclene) 815, 843, and 854 cm.$^{-1}$. Swann and Cripwell did not publish a curve for bornylene but indicated that the hydrocarbon showed strong absorption at 717 cm.$^{-1}$. We have confirmed this, and find other bands in the spectrum (Nujol) of the pure hydrocarbon at 691, 749 (but not also a band of comparable strength *ca.* 10 cm.$^{-1}$ higher; cf. camphene), 798, 841 (but not also a comparable band at 854 cm.$^{-1}$; cf. tricyclene), and 874 cm.$^{-1}$. The extremely strong 717 cm.$^{-1}$ band exhibited by bornylene made easy the identification of this hydrocarbon in admixture (even in traces) with camphene, while camphene admixed with larger proportions of bornylene was identified by its bands at 670 and 760 cm.$^{-1}$. A small proportion of tricyclene in bornylene or in camphene was identified mainly by its bands at 815 and 854 cm.$^{-1}$, or at 843 and 854 cm.$^{-1}$ respectively.

Pyrolysis of Bornyltrimethylammonium Hydroxide.—(+)-Bornyltrimethylammonium iodide (1·67 g.) was converted by the silver oxide method into an aqueous solution of quaternary hydroxide, which was evaporated at room temperature in a vacuum-desiccator. The dry waxy residue decomposed slowly at 140—160° (bath)/0·3 mm. in a distillation apparatus with a cold trap (CO_2); the quaternary base remained solid during the degradation. The distillate was treated with excess of dilute acetic acid, and the (−)-bornylene (324 mg.) was separated by filtration. After being dried between filter papers and sublimed it had m. p. 111—112° $[\alpha]_D$ −21° (Found: C, 88·0; H, 12·0. Calc. for $C_{10}H_{16}$: C, 88·2; H, 11·8%). The infrared spectrum gave no indication of presence of traces of camphene or tricyclene. Bornyldimethylamine was obtained from the acetic acid solution, being isolated as the hydrochloride (298 mg.), $[\alpha]_D$ +5·6°.

A slightly damp sample of quaternary hydroxide (from 3·2 g. of methiodide) melted at 180° (bath) and decomposed completely in 3 min. at that temperature at 0·01 mm., yielding

[18] Mousseron, Jacquier, and Zagdoun, *ibid.*, 1952, 197.
[19] Swann and Cripwell, *Ind. Chemist*, 1948, 573.

bornylene (600 mg.), m. p. 108°, $[\alpha]_D$ −19°, slightly contaminated (infrared spectrum) with camphene, and bornyldimethylamine [isolated as hydrochloride (652 mg.), a sample of which yielded the picrate, m. p. and mixed m. p. 213°].

Pyrolysis of neo*Bornyltrimethylammonium Hydroxide.*—Quaternary base from the (−)-iodide (2 g.) when treated as above at 150—160° yielded *neo*bornyldimethylamine (146 mg.) and bornylene (363 mg.), m. p. 106°, $[\alpha]_D$ −19°, containing (infrared spectrum) a little tricyclene.

Pyrolysis of a Mixture of Bornyl and neo*Bornyltrimethylammonium Hydroxides.*—Quaternary base from mixed methiodide (30% of bornyl- and 70% of *neo*bornyl-trimethylammonium iodide; 16·4 g.) was almost completely decomposed (without fusion) when heated at 150—210°/0·3 mm. during several hours. The residue in the pyrolysis flask was treated with potassium iodide and sodium hydroxide solutions and extracted with chloroform, evaporation of which yielded nearly pure bornyltrimethylammonium iodide (135 mg.), m. p. (from ether–methanol) 277° (following decomp. at 270°), $[\alpha]_D$ −2·4°. The infrared absorption curve (potassium bromide disc) and the *X*-ray powder photograph were identical with those from pure bornyltrimethylammonium iodide ($[\alpha]_D$ −3·7°) and entirely different from those of the *neo*-epimer ($[\alpha]_D$ −34°). The distillate was separated into basic (1·21 g.) and neutral (2·4 g.) fractions. The basic fraction, $[\alpha]_D$ +3·2° (Found: C, 79·9; H, 12·8; N, 7·6. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%), yielded a hydrochloride, $[\alpha]_D$ −2·4° and appeared from the optical rotatory data to consist of 70—80% of bornyl- and 20—30% of *neo*bornyl-dimethylamine; the mixture with picric acid gave bornyldimethylamine picrate, m. p. 213—214°. After further distillation the neutral fraction had m. p. 109—110°, $[\alpha]_D$ −20°; purification by Henderson and Caw's method [12] (hydrogen peroxide–acetic acid) gave bornylene, m. p. 111—112°, $[\alpha]_D$ −21°, the infrared spectrum of which indicated no contamination with camphene or tricyclene.

Degradation of (−)-*Bornyltrimethylammonium Iodide in Alkaline Glycol.*—A mixture of the quaternary salt (2·5 g.) and ethylene glycol (33 c.c.) was treated with potassium hydroxide (13 g.) in water (13 c.c.), and the whole reduced to one-third of the volume by distillation. The distillate contained (+)-bornyldimethylamine (1·37 g.), $[\alpha]_D$ +26°, n_D^{26} 1·4772 (Found: C, 79·7; H, 12·8; N, 8·1. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%), from which the picrate, m. p. 214°, was obtained. No hydrocarbon fraction was obtained.

Degradation of (−)-neo*Bornyltrimethylammonium Iodide in Alkaline Glycol.*—The quaternary salt (800 mg.) when treated as above gave the tertiary base (72 mg.; identified as the picrate, m. p. 194°) separated with dilute acetic acid from a neutral fraction (225 mg.), m. p. 49°, identified as camphene by its infrared spectrum which indicated contamination with a little bornylene and tricyclene. A more detailed examination of the hydrocarbon was made on samples obtained from degradations in alkaline glycol of the more readily accessible mixtures of bornyl- and *neo*bornyl-trimethylammonium iodide (following paragraph); it is evident that the camphene from such experiments is derived from the (−)-*neo*-quaternary salt.

Degradation of Mixtures of Bornyl- and neo*Bornyl-trimethylammonium Iodides in Alkaline Glycol.*—(*a*) A mixture ($[\alpha]_D$ −18·5°; approximately equimolar) of the methiodides (3·02 g.), when completely decomposed as described above, yielded (+)-camphene (350 mg.), m. p. 49°, $[\alpha]_D$ +104° (in EtOH), +112° (in C_6H_6) (Found: C, 88·3; H, 11·8. Calc. for $C_{10}H_{16}$: C, 88·2; H, 11·8%). The infrared spectrum indicated presence of traces of tricyclene and bornylene. For (+)-camphene prepared by the usual type of elimination reaction a range of optical rotatory values has been recorded up to +99·6° (in EtOH), +107·7° (in C_6H_6), and +103·9° (in Et_2O); [20] the more elaborate procedure of Bain and his collaborators [21] yielded (−)-camphene considered by these authors to be optically pure; it had m. p. 49·1°, $[\alpha]_D$ −113·5° (in Et_2O), −117·5° (in toluene). Our basic reaction product (880 mg.) (Found: C, 79·6; H, 12·7; N, 7·6. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%) had n_D^{25} 1·4778, $[\alpha]_D$ +15°; it yielded a hydrochloride, $[\alpha]_D$ +0·2°, and on treatment with picric acid afforded bornyldimethylamine picrate, m. p. 213°. The indications are that the recovered tertiary base contains *ca.* 10—20% of *neo*bornyl- and 80—90% of bornyl-dimethylamine.

(*b*) Decomposition of a methiodide mixture ($[\alpha]_D$ −16°; 610 mg.) by distillation of its solution in glycol containing only 1 mol. of potassium hydroxide yielded camphene (42 mg.), $[\alpha]_D$ +98°, and bornyldimethylamine (170 mg.), isolated as the hydrochloride, $[\alpha]_D$ +10°.

(*c*) An approximately equimolar mixture of methiodide ($[\alpha]_D$ −18·5°; 1·01 g.) was heated under reflux with potassium hydroxide (0·45 g.) in glycol (8 c.c.) and water (2 c.c.) for 5 min.

[20] Rodd (Ed.), "Chemistry of Carbon Compounds," Elsevier, Amsterdam, 1953, Vol. IIB, p. 586.
[21] Bain, Best, Hampton, Hawkins, and Kitchen, *J. Amer. Chem. Soc.*, 1950, **72**, 3124.

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at 186° (bath); the mixture was cooled, extracted with ether, treated with saturated aqueous potassium iodide (100 c.c.), and extracted with chloroform. The chloroform extract contained nearly pure (−)-bornyltrimethylammonium iodide (317 mg.), $[\alpha]_D$ −3·0°, m. p. 284°.

(*d*) Mixed methiodides ($[\alpha]_D$ −18°; 4·7 g.), when heated in glycol (50 c.c.) with potassium hydroxide (9·5 g.) at 100° for 2 hr., yielded a tertiary basic mixture isolated as hydrochloride ($[\alpha]_D$ −7·6°; 252 mg.) and some camphene; treatment of the glycol solution with potassium iodide and extraction with chloroform resulted in the recovery of mixed methiodides ($[\alpha]_D$ −15·7°; 3·6 g.). These figures indicate that 23% of the methiodide mixture was decomposed, that the original and the final methiodide mixtures contained respectively 52% and 59% of the bornyl epimer, and that the hydrochloride mixture isolated contained 77% of the bornyl epimer. It may be calculated that 0·32 g. of bornyltrimethylammonium iodide is decomposed; as this yields only tertiary base, the recovered hydrochloride should contain 83% of the bornyl epimer, so that the internal consistency of the figures is satisfactory for an essentially qualitative experiment. A further experiment, in which 16% of the original, approximately equimolar, methiodide mixture was allowed to decompose, again indicated the preferential loss of methanol from the bornyl epimer.

Competition of Bornyl- and neo*Bornyl-dimethylamine for Methyl Iodide.*—When a mixture of tertiary amines (4·3 g.) containing (optical rotation) 62% of the bornyl epimer was treated in ether (100 c.c.) with methyl iodide (2·4 c.c.) at 5° the first fraction (110 mg.) of methiodide which separated contained (optical rotation) 87% of bornyltrimethylammonium iodide. Neither quaternary iodide is appreciably soluble in ether.

Stability of Camphene, Bornylene, and Tricyclene to the Reaction Conditions.—None of the hydrocarbons was altered appreciably in infrared spectrum, m. p., or specific rotation when refluxed for some time with alkaline glycol and then recovered by distillation. Tricyclene was likewise unaltered overnight in glacial acetic acid at room temperature. These experiments indicate that camphene or bornylene, when isolated in the above experiments, is not an artefact derived from either of the other hydrocarbons by isomerisation. Camphene, m. p. 47°, $[\alpha]_D$ +101°, was unaltered on being heated with water at 150° for 12 hr. with or without addition of one mol. of trimethylamine hydriodide; this fact is relevant to the interpretation of the results described in the following paragraph.

Degradation of Mixed Methiodides in Neutral Aqueous Solution.—An approximately equimolar mixture of (−)-bornyl- and (−)-*neo*bornyl-trimethylammonium iodides ($[\alpha]_D$ −17°; 2 g.) in water (14·5 c.c.) was heated in a sealed tube at 160° for 12 hr.; the mixture was then cooled and treated with dilute acetic acid, and the solid (202 mg.) was filtered off. This had m. p. 49—50°, raised to 54° on sublimation, $[\alpha]_D$ +52·5°; it was (infrared spectrum) essentially camphene (Found: C, 88·5; H, 11·3. Calc. for $C_{10}H_{16}$: C, 88·2; H, 11·8%); it contained a little tricyclene, but there was an unidentified band at 789 cm.$^{-1}$. There was no trace of the powerful 717 cm.$^{-1}$ band exhibited by bornylene, and the tricyclene bands at 843 and 854 cm.$^{-1}$ were just clearly visible, and very much weaker than in the spectrum of a 1 : 1 mixture of (+)-camphene and tricyclene. The low optical rotation of the degradation hydrocarbon is therefore not due in the main to its tricyclene content. The filtration apparatus and acetic acid filtrate when washed with benzene yielded a further 106 mg. of hydrocarbon, as estimated from the optical rotation of the extract.

The filtrate from the hydrocarbon was evaporated to dryness, and the residue was dissolved in aqueous sodium hydroxide and extracted several times with ether. Addition of picric acid to the ether extract yielded trimethylamine picrate (370 mg.), m. p. and mixed m. p. 216° depressed to *ca.* 185° on admixture with bornyldimethylamine picrate (Found: C, 37·2; H, 4·3; N, 19·3. Calc. for $C_9H_{12}O_7N_4$: C, 37·6; H, 4·2; N, 19·4%). Saturation of the alkaline solution with potassium iodide and extraction with chloroform yielded bornyltrimethylammonium iodide (910 mg.), m. p. and mixed m. p. 280°, hot aqueous solutions of which therefore decompose much more slowly than those of the *neo*-epimer.

Degradation of Aqueous (−)-Bornyltrimethylammonium Iodide.—A saturated aqueous solution of (−)-bornyltrimethylammonium iodide (1 g.) was heated at 210° for 5 days, yielding an oily neutral insoluble fraction (360 mg.) and a mixture (640 mg.) of bornyldimethylamine hydriodide and (presumably) trimethylamine hydriodide which on basification, extraction with ether, evaporation of the extract, and treatment of the residue with ethereal picric acid gave bornyldimethylamine picrate (400 mg.), m. p. and mixed m. p. 213—214°. The alkaline aqueous solution on saturation with potassium iodide and extraction with chloroform gave

unchanged bornyltrimethylammonium iodide (74 mg.), m. p. and mixed m. p. 281°. The neutral oil partially crystallised; the solid, m. p. 45°, was identified by its infrared spectrum as camphene containing a little tricyclene.

Degradation of (−)-neo*Bornyltrimethylammonium Iodide in Aqueous Solutions of Varying Alkali Concentration.*—(*a*) A solution of the methiodide (200 mg.) in aqueous 10% potassium hydroxide (6 c.c.) was heated in a sealed tube at 155° for 12 hr., cooled, and extracted with benzene. The extract was shaken with dilute hydrochloric acid, and the mixture evaporated to dryness. The residual hydrochloride (12 mg.) was converted into the picrate, m. p. 216°, alone or mixed with authentic trimethylamine picrate of m. p. 216°, but depressed to *ca.* 175° on admixture with *neo*bornyldimethylamine picrate (m. p. 194°). The reaction mixture contained no residual methiodide.

(*b*) Four sealed tubes each containing methiodide (*ca.* 30 mg.) and varying amounts of potassium hydroxide in water (1·8 c.c.) were heated at 140° for 40 min. and cooled. The contents of each tube were treated with aqueous 30% potassium hydroxide (10 c.c.) and saturated with potassium iodide, and all residual methiodide was extracted with chloroform (4 × 10 c.c.); the chloroform extract was evaporated and the residue washed (with negligible loss in weight) with ether. The recovered quaternary iodide was identified by its infrared spectrum. The following results were obtained:

Tube no.	1	2	3	4
Weight of methiodide taken (mg.)	31·15	28·7	33·0	29·75
Mols. of alkali	70	35	2	0
Weight of methiodide recovered (mg.)	11·5	11·95	12·25	9·6
Reaction (%)	63	58·5	63	67·5

Pyrolysis of Bornyl- and neo*Bornyl-trimethylammonium Iodide.*—When the *neo*-methiodide was heated at 170—190°/0·1 mm. for 3 hr., it was apparently completely decomposed into trimethylamine hydriodide (which partly sublimed during the reaction), m. p. 230—240° (Found: I, 68·3. Calc. for $C_3H_{10}NI$: I, 67·9%), the infrared spectrum of which (in a potassium bromide disc) was identical with that from an authentic specimen, and camphene, m. p. 40°, containing (infrared spectrum) some tricyclene.

The epimeric quaternary salt lost no weight at 200°/17 mm. in 70 min., but when kept at 250°/0·005 mm. for 8 hr. afforded a mixture of bornyldimethylamine and (presumably) trimethylamine hydriodides, from which the picrate of the former base was prepared (m. p. and mixed m. p. 215°), and a small quantity of neutral oily distillate, which was dissolved in carbon disulphide. The only bands in the infrared spectrum of this solution sufficiently prominent for characterisation were at 670 and 877 $cm.^{-1}$; these correspond in position to the two strongest camphene bands.

Degradation of (+)-*Bornyldimethylamine Oxide.*—(+)-Bornyldimethylamine (450 mg.) in methanol (40 c.c.) was treated with 30% hydrogen peroxide (4 c.c.), the solution was refluxed for 14 hr., and excess of peroxide was then decomposed by treatment with manganese dioxide. The crude crystalline ether-insoluble oxide had m. p. 76—82°, $[\alpha]_D$ +3·7°; it was characterised as the *picrate*, needles (from methanol), m. p. 225° (decomp.), depressed to <200° on admixture with bornyldimethylamine picrate (Found: C, 50·8; H, 6·4; N, 13·3. $C_{18}H_{26}O_8N_4$ requires C, 50·7; H, 6·2; N, 13·1. Calc. for $C_{18}H_{26}O_7N_4$: C, 52·7; H, 6·4; N, 13·7%).

The crude amine oxide (163 mg.), when distilled with ethylene glycol, yielded volatile neutral and basic products. The former (30 mg.) had m. p. 102—104°, $[\alpha]_D$ −20° ± 5° (microtube), and was identified (infrared spectrum) as bornylene containing some tricyclene and a trace (just visible band at 670 $cm.^{-1}$) of camphene. An ether extract of the basic product was washed with water, the ether was evaporated, and the residual bornyldimethylamine (83 mg.), $[\alpha]_D$ +34°, n_D^{25} 1·4778 (Found: C, 79·4; H, 12·6; N, 7·5. Calc. for $C_{12}H_{23}N$: C, 79·5; H, 12·8; N, 7·7%), was characterised as the picrate, m. p. 212—213°.

Pyrolysis of the amine oxide at 120° (bath)/0·4 mm. also yielded crude bornylene, m. p. 105—106°, $[\alpha]_D$ −16°, and tertiary base (hydrochloride, $[\alpha]_D$ +9°); the amine oxide tended to sublime under these conditions.

Degradation of (−)-neo*Bornyldimethylamine Oxide.*—The crude oxide, prepared as described above from the (−)-tertiary base, had m. p. 66—70°, $[\alpha]_D$ −35°; it was characterised as the *picrate*, m. p. 180°, not in this case depressed on admixture with the tertiary amine picrate of m. p. 194° (Found: C, 50·5; H, 6·3; N, 13·1. $C_{18}H_{26}O_8N_4$ requires C, 50·7; H, 6·2; N, 13·1. Calc. for $C_{18}H_{26}O_7N_4$: C, 52·7; H, 6·4; N, 13·7%).

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The amine oxide (180 mg.) was distilled with ethylene glycol, and the distillate was examined as described above. It contained *neo*bornyldimethylamine (16 mg.) identified as the picrate, m. p. and mixed m. p. 194°. The neutral product, after sublimation, had m. p. 96°, $[\alpha]_D$ 0° ± 5° (micro-tube); the infrared absorption curve indicated bornylene with some admixture with camphene, the 670 and 760 cm.$^{-1}$ bands of the latter hydrocarbon being prominent. The m. p.[6] and $[\alpha]_D$ of the hydrocarbon mixture (Found: C, 88·0; H, 12·2. Calc. for $C_{10}H_{16}$: C, 88·2; H, 11·8%) suggest that it contains *ca.* 20% of camphene.

Pyrolysis of the amine oxide at 120° (bath)/0·4 mm. gave similar products, the hydrocarbon (Found: C, 88·0; H, 11·8%) again having m. p. 96°.

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THE UNIVERSITY, SHEFFIELD. [*Received, March 11th*, 1958.]

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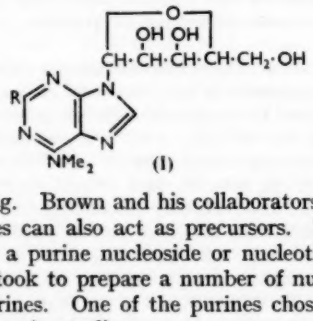
564. *The Synthesis of 6-Dimethylamino-9-β-D-ribofuranosylpurine-5′ phosphate.*

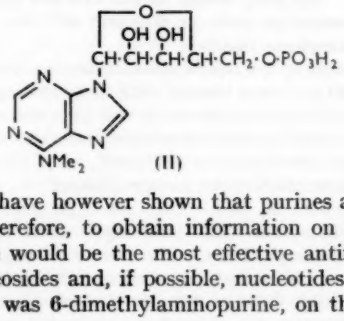
By K. J. M. ANDREWS and W. E. BARBER.

6-Dimethylamino-9-β-D-ribofuranosylpurine-5′ phosphate has been synthesised, from the nucleoside, by using *O*-benzylphosphorous *OO*-diphenylphosphoric anhydride. Ribofuranosides derived from 6-dimethylamino-8-azapurine and 6-dimethylamino-2-methylthio-8-azapurine are also described.

ALTHOUGH the antimetabolite theory has not led to a generally useful chemotherapeutic agent for cancer, results on experimental tumours with such compounds as 6-mercaptopurine and 8-azaguanine have stimulated searches for potent purine and pyrimidine antimetabolites. Evidence has been given that purine ribotides, the precursors of nucleic acids, are synthesised from glycinamide ribotide with the gradual building up of the



(I)



(II)

purine ring. Brown and his collaborators [2] have however shown that purines and purine nucleosides can also act as precursors. Therefore, to obtain information on whether a purine or a purine nucleoside or nucleotide would be the most effective antimetabolite we undertook to prepare a number of nucleosides and, if possible, nucleotides of known active purines. One of the purines chosen was 6-dimethylaminopurine, on the basis of the puromycin studies.

Our first objective, 6-dimethylamino-9-β-D-ribofuranosylpurine (I; R = H) was prepared *via* the 2-methylthio-compound by Kissman, Pidacks, and Baker,[3] and our synthesis, performed independently, varied only in detail. The preparation of tetra-*O*-acetyl-β-D-ribofuranose, required for the formation of the acetochloro-sugar used in the

[1] Goldthwait, Peabody, and Greenberg, *J. Amer. Chem. Soc.*, 1954, **76**, 5258; Hartman, Levenberg, and Buchanan, *ibid.*, 1955, **77**, 501; Greenberg and Spilman, *J. Biol. Chem.*, 1956, **219**, 411; Levenberg and Melnick, *Fed. Proc.*, 1956, **15**, 117.

[2] Brown, Roll, and Weinfeld, "Phosphorus metabolism," Johns Hopkins Univ. Press, Baltimore, 1952, Vol. II, p. 385.

[3] Kissman, Pidacks, and Baker, *J. Amer. Chem. Soc.*, 1954, **77**, 18.

synthesis, can present some difficulty.[3] We found that hand-separation combined with one or two recrystallisations (see below) was the least laborious method of preparing 50—100 g. batches.

6-Dimethylamino-2-methylthio-(?)9-ribofuranosyl-8-azapurine* and 6-dimethylamino-9-ribofuranosyl-8-azapurine were also synthesised, and the 2′ : 3′-*O*-benzylidene derivative of 6-dimethylamino-9-β-D-ribofuranosylpurine was prepared.

The preparation of 6-dimethylamino-9-β-D-2′ : 3′-*O*-*iso*propylideneribofuranosylpurine, with zinc chloride as catalyst, gave *ca.* 25% yields, but use of toluene-*p*-sulphonic acid (cf. Baker and Schaub [4] who used ethanesulphonic acid) led to a 71% yield, and the corresponding 2-methylthio-compound was obtained in 90% yield.

In an attempt to synthesise 6-dimethylamino-9-β-D-ribofuranosylpurine-5′ phosphate (II), dibenzyl phosphorochloridate was first used with the 2′ : 3′-*O*-*iso*propylidene and the 2′ : 3′-*O*-benzylidene derivative (cf. the phosphorylation of *iso*propylideneadenosine [5]); but, although after removal of the protecting groups a small amount of organic phosphate was detected by paper chromatography none could be isolated. *O*-Benzylphosphorous *OO*-diphenylphosphoric anhydride [6] was then used with the 2′ : 3′-*O*-*iso*propylidene derivative. The crude 5′-phosphite was converted into the phosphorochloridate, then into the benzyl hydrogen phosphate by hydrolysis, and the protecting groups were removed in the usual way (cf. the synthesis of deoxyguanosine-5′ phosphate [7]). It was essential not to hydrolyse the *iso*propylidene group (by prolonged storage in acid) until after hydrogenolysis of the benzyl group, as otherwise hydrogenolysis was inhibited and crystalline material was not obtained.

Kissman *et al.*[3] reported that 6-dimethylamino-9-β-D-ribofuranosylpurine was active against the transplanted mammary adenocarcinoma of the C_3H mouse. Studies on this compound by Dr. Grunberg in the laboratories of Hoffmann-La Roche, Inc., Nutley, New Jersey, showed possibly a slight but not an appreciable activity against the Sarcoma 180 strain of transplantable mouse tumour and the result, on a molar basis, was of the same order as for the purine. The 5′-phosphate is under investigation.

Experimental

6-Dimethylamino-2-methylthio-9-β-D-ribofuranosylpurine (I; R = MeS).—6-Dimethylamino-2-methylthiopurine [8] (16 g.), suspended in ethanol (100 ml.), was treated with aqueous 2N-sodium hydroxide solution (38 ml.). To the solution formed on warming was added a solution of mercuric chloride (22 g.) in ethanol (100 ml.). After cooling, the precipitated solid was washed with water, ethanol, and ether and dried *in vacuo* (P_2O_5) (yield 25 g., 73·5%).

This mercuric chloride complex (13·5 g.) and " Hyflo supercel " (13·5 g.) were suspended in chlorobenzene (250 ml.) and dried by distillation of half the solvent, with stirring. Acetochlororibofuranose was prepared from tetra-*O*-acetyl-β-D-ribofuranose † (12 g.) and ethereal hydrogen chloride [9] (120 ml.; saturated at 0°). The solvent was evaporated *in vacuo*, and the residual gum was dissolved in dry toluene and re-evaporated *in vacuo*; all evaporations were at low bath-temperature. The acetochlororibofuranose, dissolved in dry chlorobenzene (100 ml.), was added to the suspension of the purine compound and the mixture was stirred and heated under reflux for 3 hr. The mixture was filtered hot and the solids were extracted with hot chloroform until the extracts were colourless. The combined filtrates were evaporated *in vacuo*, and the residue was dissolved in chloroform (150 ml.). The chloroform solution was

* Although it has been proved that 6-substituted 2-methylthiopurines give 9-β-D-ribofuranosylpurines it is not yet safe to assume that substitution in similar 8-azapurines is also at the 9-position.

† When a solution of the crude product evaporates in a large dish in the air the furanose and the pyranose compounds form large crystals which are easily recognised and separated by hand. One or two recrystallisations then give pure material.

[4] Baker and Schaub, *ibid.*, 1955, **77**, 5900.
[5] Baddiley and Todd, *J.*, 1947, 650.
[6] Corby, Kenner, and Todd, *J.*, 1952, 3669.
[7] Hayes, Michelson, and Todd, *J.*, 1955, 808.
[8] Baker, Joseph, and Schaub, *J. Org. Chem.*, 1954, **19**, 631.
[9] Davoll, Lythgoe, and Todd, *J.*, 1948, 967.

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washed with 30% aqueous potassium iodide (2 × 50 ml.) and water (100 ml.). The chloroform phase was dried by filtration, treated with charcoal, filtered, and evaporated *in vacuo*, yielding a yellow-brown glass (16·3 g.).

The glass was dissolved in dry methanol (25 ml.), and methanolic 5N-ammonia (200 ml.) was added. The solution was left at atmospheric temperature for 24 hr., then evaporated *in vacuo*. A yellow oil was obtained which solidified on trituration with water and, recrystallised from water (*ca.* 200 ml.), had m. p. 174—175°, $[\alpha]_D^{20}$ −43·6° (*c* 1·6 in MeOH) (3·3 g., 40%) [a second crop (0·9 g.) had m. p. 173—174°] (Found, in material dried at 110° *in vacuo*: C, 46·0; H, 5·8; N, 20·6. Calc. for $C_{13}H_{19}O_4N_5S$: C, 45·7; H, 5·6; N, 20·5%).

6-*Dimethylamino*-9-β-D-*ribofuranosylpurine* (I; R = H).—6-Dimethylamino-2-methylthiopurine mercuric chloride complex (32 g.) was treated with acetochlororibofuranose [from tetra-*O*-acetylribofuranose (28 g.)] as in the previous experiment, except that the mixture was heated for 3½ hr. After evaporation of the chloroform solution, the crude 6-dimethylamino-2-methylthio-9-β-D-2′ : 3′ : 5′-*O*-triacetylribofuranosylpurine was dissolved in methanol (1·5 l.), freshly prepared Raney nickel (*ca.* 80 g.; prepared according to Mozingo's directions [10] with the final heating at 50°) was added, and the mixture was stirred and heated under reflux for 1 hr. The nickel was removed through a pad of "Hyflo supercel," and was washed with boiling methanol (1 *l.*). The filtrates were evaporated *in vacuo*, yielding a yellow gum. (Ultraviolet absorption showed desulphurisation to be complete by the absence of a maximum at 248 mμ.) The gum was treated in methanol (300 ml.) with methanolic N-sodium methoxide (3 ml.) and refluxed for 1 hr. (If the pH was then less than 8, further sodium methoxide was added and heating continued for a further ½ hr.) The solution was evaporated *in vacuo* (crystals which came out before evaporation was complete were collected), and the residue dissolved in a few ml. of water, and this solution treated with boiling acetone. The acetone solution was evaporated *in vacuo*. The residual oil, after two evaporations *in vacuo* with acetone, solidified and the solid was collected, combined with the crystals obtained from the methanol evaporation, and recrystallised from water (*ca.* 10 ml.) and acetone (*ca.* 150 ml.). The white fluffy needles (9·8 g.) were filtered off, washed with acetone, and dried *in vacuo* (P_2O_5); they had m. p. 182—183°. Evaporation of the mother-liquors and recrystallisation of the residue yielded a further 2·3 g. with the same m. p. {total yield 57%; $[\alpha]_D^{20}$ −58·5° (*c* 2·3 in H_2O)} (Found, in material dried *in vacuo* at 110: C, 48·5; H, 5·7; N, 23·6. Calc. for $C_{12}H_{17}O_4N_5$: C, 48·7; H, 5·8; N, 23·8%).

6-*Dimethylamino*-9-(2′ : 3′-O-iso*propylidene*-β-D-*ribofuranosyl*)*purine*.—6-Dimethylamino-9-β-D-ribofuranosylpurine (9 g.), dry acetone (450 ml.), and anhydrous copper sulphate (36 g.) were stirred and toluene-*p*-sulphonic acid (36 g.) in dry acetone (200 ml.) was added. The mixture was stirred for ½ hr. The solids were removed and were washed with acetone (2 × 200 ml.). The filtrate was poured into a solution of sodium carbonate (30 g., anhyd.) in water (*ca.* 400 ml.), which was then extracted with chloroform (3 × 400 ml.). The chloroform phase was evaporated *in vacuo*, yielding a solid which, recrystallised from ethanol, gave the *product* as needles (6·8 g., 73%), m. p. 176—177° (Found, in material dried at 110° *in vacuo*: C, 53·7; H, 6·5; N, 21·0. $C_{15}H_{21}O_4N_5$ requires C, 53·7; H, 6·3; N, 20·9%).

6-*Dimethylamino*-9-β-D-*ribofuranosylpurine*-5′ *phosphate* (cf. II).—To benzyl dihydrogen phosphite (4·07 g.) in dry benzene (33 ml.) diphenyl phosphorochloridate (4·9 ml.) was added. The solution was stirred and triethylamine (3·33 ml.) in dry benzene (33 ml.) was added during *ca.* 10 min. The mixture was stirred for 1 hr. at room temperature and the triethylamine hydrochloride formed was removed. To the filtrate was added 6-dimethylamino-9-(2′ : 3′-*O*-*iso*propylidene-β-D-ribofuranosyl)purine (5 g., dried *in vacuo* at 100° over P_2O_5 for 5 hr.) and 2 : 6-lutidine (2·7 ml.). The mixture was stirred for ½ hr. at room temperature, then filtered and evaporated *in vacuo* at room temperature. The residue was dissolved in chloroform (100 ml.) and washed with water (100 ml.), saturated sodium hydrogen carbonate solution (100 ml.) and water (100 ml.). The chloroform solution was dried by filtration and evaporated *in vacuo*, at room temperature, yielding crude 6-dimethylamino-9-(2′ : 3′-*O*-*iso*propylidene-β-D-ribofuranosyl)purine-5′ benzyl hydrogen phosphite as a pale yellow oil (7·8 g.).

The phosphorochloridate was formed by stirring the oil in dry benzene (80 ml.) with *N*-chlorosuccinimide (2 g.) at room temperature for 2 hr. The resultant solution was stirred with acetonitrile (80 ml.) and saturated aqueous sodium hydrogen carbonate solution (160 ml.) for 6 hr. and kept for a further 9 hr. The aqueous phase was separated and filtered and the

[10] Mozingo, *Org. Synth.*, 1941, **21**, 15.

acetonitrile removed by evaporation *in vacuo* at <30°. Half of the residual aqueous solution was set aside and the other half was cooled in ice-water and acidified with dilute hydrochloric acid to pH *ca.* 2 and extracted with chloroform (5 × 50 ml.). The combined chloroform extracts were dried by filtration and evaporated *in vacuo* at room temperature. The gummy residue (2·2 g.) was immediately dissolved in ethanol (100 ml.), and water (100 ml.) was added. The solution was treated with charcoal and the filtered solution was hydrogenated at atmospheric pressure over palladium oxide (0·5 g.), and 10% palladium–charcoal (0·5 g.) [previously reduced in 50% ethanol (50 ml.)]; 100 ml. of hydrogen were absorbed in 2 hr. The catalyst was removed and the filtrate evaporated *in vacuo*. The residue was dissolved in water (3 ml.) and boiled for *ca.* 2 min. to remove the *iso*propylidene group. After cooling, acetone was added to turbidity and the solution was set aside at 0° for 3 days during which crystals were deposited. The crystals (0·6 g., 19·5%) were collected, washed with acetone, and dried *in vacuo* over P_2O_5; they had m. p. 223° (decomp.). Recrystallisation from water (15 ml.) and acetone yielded the *phosphate* (0·5 g.), m. p. 225° (decomp.), $[\alpha]_D^{20}$ −51° (*c* 1·98 in H_2O), $\lambda_{max.}$ 268 mμ (ε 18,300). The compound showed a single spot of R_P 0·39 (ultraviolet-absorbent and phosphorus-containing) on a paper chromatogram, with propan-1-ol–ammonia (*d* 0·88)–water (60 : 30 : 10) as solvent ascending on Whatman No. 1 paper for 17 hr. at room temperature (Found, in material dried *in vacuo* at 110°: C, 38·9; H, 5·1; N, 18·8; P, 8·1. $C_{12}H_{18}O_7N_5P$ requires C, 38·4; H, 4·8; N, 18·7; P, 8·3%).

6-*Dimethylamino*-2-*methylthio*-8-*azapurine*.—4 : 5-Diamino-6-dimethylamino-2-methylthiopyrimidine (10 g.) was partially dissolved in 2M-sodium acetate (400 ml.), 2N-hydrochloric acid (25 ml.), and acetic acid (5 ml.) at 80°. Sodium nitrite (20 g.) in water (200 ml.) was added, and the mixture kept at 95° for ½ hr., then cooled, and filtered. The solid was washed with water and crystallised from ethanol (*ca.* 500 ml.) (charcoal). 6-*Dimethylamino*-2-*methylthio*-8-*azapurine* crystallised in colourless needles (8·5 g.), m. p. 263° [the mother-liquors gave a second crop (0·8 g.), m. p. 262°] (Found, in material dried *in vacuo* at 110°: C, 40·1; H, 4·9; N, 40·4. $C_7H_{10}N_6S$ requires C, 40·0; H, 4·8; N, 40·0%).

6-*Dimethylamino*-2-*methylthio*-(?)9-β-D-*ribofuranosyl*-8-*azapurine*.—The 6-dimethylamino-2-methylthio-8-azapurine mercuric chloride complex (prepared in a similar way to the complex described above) (12 g.) and acetochlororibofuranose (from 9·5 g. of tetra-*O*-acetyl-β-D-ribofuranose) were caused to react by the method previously described. Deacetylation of the crude tri-*O*-acetylribosyl compound with methanolic ammonia yielded a solid *purine* on trituration with water; recrystallised twice from water this had m. p. 146·5—148° (yield 49·5%) (Found, in material dried *in vacuo* at 100°: C, 41·5; H, 5·4; N, 24·7. $C_{12}H_{18}O_4N_6S$ requires C, 42·0; H, 5·3; N, 24·6%).

6-*Dimethylamino*-9-β-D-*ribofuranosyl*-8-*azapurine*.—Dimethylamino-2-methylthio-9-β-D-ribofuranosyl-8-azapurine (400 mg.) was stirred in ethanol (100 ml.) with Raney nickel (*ca.* 3 g.) under reflux for 1 hr. The mixture was filtered hot through " Hyflo supercel," and the solids were extracted with boiling ethanol (250 ml.). The filtrates were evaporated *in vacuo*. The residue (150 mg.) crystallised on trituration with ether (m. p. 199—200°). Recrystallisation from a little water–ethanol gave a *product*, m. p. 216° (70 mg., 21%) (Found, in material dried *in vacuo* at 110°: C, 44·5; H, 5·7; N, 28·2. $C_{11}H_{16}O_4N_6$ requires C, 44·6; H, 5·4; N, 28·4%).

6-*Dimethylamino*-9-(2′ : 3′-O-*benzylidene*-β-D-*ribofuranosyl*)*purine*.—Zinc chloride (750 mg.), benzaldehyde (3·7 ml.; dry), and 6-dimethylamino-9-β-D-ribofuranosylpurine (290 mg.) were shaken for 24 hr., in which dissolution was effected. The solution was poured into dry ether (50 ml.), and the precipitate was collected, washed with dry ether, dissolved in " Ethyl cellosolve " (4·3 ml.), and treated with aqueous 2N-sodium hydroxide (3·2 ml.). After 10 min., the solid was removed and was washed with hot " Ethyl cellosolve." The filtrate was evaporated *in vacuo*. On trituration with water, the resulting oil crystallised. The *compound* (155 mg.) washed with water and dried *in vacuo* (P_2O_5), had m. p. 159—162°. From the filtrate and washings, by evaporation, starting material (80 mg.) was obtained. The product was recrystallised twice from ethanol, the m. p. rising to 172° (yield 100 mg., 34%) (Found, in material dried *in vacuo* at 110°: C, 59·4; H, 5·7; N, 17·8. $C_{19}H_{21}O_4N_5$ requires C, 59·5; H, 5·8; N, 18·3%).

The authors thank Dr. A. L. Morrison for his interest.

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XUM

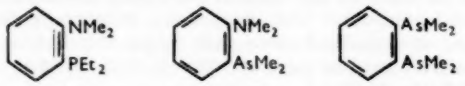
565. *The Constitution of Complex Metallic Salts. Part XVIII.*[1] *The Chelated Metallic Derivatives of* NNN'N'-*Tetramethylethylenediamine and of* 1 : 4-*Dimethylpiperazine.*

By Frederick G. Mann and H. R. Watson.

It is shown that the two diamines named in the title form stable chelated compounds of type [diamine MX_2], where X = halogen, with Pd^{2+}, Pt^{2+}, and Ir^{2+} ions, and the first diamine forms similar but less stable compounds with Cu^{2+} and Cd^{2+} ions. Compounds having two molecules of these diamines chelated to one metallic atom could not be prepared. These are apparently the first recorded examples of a simple ditertiary amine forming stable chelated metallic compounds. The composition, structure, and stability of these compounds are discussed.

It is well known that simple tertiary aliphatic amines very rarely co-ordinate stably with metallic salts, but that the co-ordinating power of a tertiary amino-group may be considerably reinforced if the group forms part of a molecule having a second strongly co-ordinating group in such a position that the two groups can form a chelating unit. For example, the detailed study of the co-ordinated palladium derivatives of *o*-dimethylaminophenyldiethylphosphine [1] (I) and *o*-dimethylaminophenyldimethylarsine [2] (II) has shown that these compounds form stable chelated palladium compounds, but that the advent of a strongly co-ordinating group such as the iodide ion almost certainly ruptures the N–Pd link, the amino-group becoming free and the iodine atom co-ordinating to the metal.

The co-ordinating groups in the compounds (I) and (II), and also in the strongly chelating *o*-phenylenebis(dimethylarsine) (III),[3,4] are however rigidly held in almost the ideal position for co-ordinated 5-membered ring formation.



(I) (II) (III)

A similar factor undoubtedly influences the co-ordination of 2 : 2' : 2''-triaminotriethylamine [5] (IV), 3 : 3' : 3''-triaminotripropylamine [6] (V), and *NNN'N'*-tetra-(2-aminoethyl)ethylenediamine [7] (VI), the tertiary amino-groups of which co-ordinate stably to metals: co-ordination of the primary amino-groups in the compounds (IV), (V), and (VI), around, for example, the 6-co-ordinate octahedron must bring the tertiary amino-groups into the precise position for co-ordination, and the stability of the whole complex will be enhanced by co-ordination of all available groups.

$N(CH_2{\cdot}CH_2{\cdot}NH_2)_3$ $N(CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2)_3$ $(H_2N{\cdot}CH_2{\cdot}CH_2)_2N{\cdot}CH_2{\cdot}CH_2{\cdot}N(CH_2{\cdot}CH_2{\cdot}NH_2)_2$

(IV) (V) (VI)

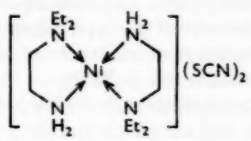
This factor cannot apply so powerfully to the *N*-alkylethylenediamines, in which the flexibility of the molecule enables the distance separating the nitrogen atoms to vary over a wide range. Yet Mann [8] has shown that *NN*-diethylethylenediamine (VII; R = Et)

[1] Part XVII, Mann and Watson, *J.*, 1957, 3950.
[2] Mann and Stewart, *J.*, 1955, 1269.
[3] Chatt and Mann, *J.*, 1939, 1622.
[4] Nyholm, *J.*, 1950, 851 *et seq.*
[5] Mann and Pope, *Proc. Roy. Soc.*, *A*, 1925, **109**, 444; *J.*, 1926, **129**, 482; Mann, *J.*, 1929, 409.
[6] Mann and Pope, *J.*, 1926, 489.
[7] Gauss, Moser, and Schwarzenbach, *Helv. Chim. Acta*, 1952, **35**, 2359; Schwarzenbach and Moser, *ibid.*, 1953, **36**, 581.
[8] Mann, *J.*, 1927, 2904.

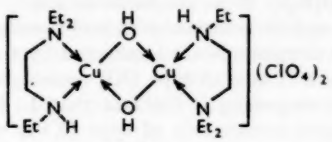
gives stable nickel salts of type (XI), and Pfeiffer and Glaser[9] have shown that this diamine, and also *NN'*-diethylethylenediamine (VIII; R = Et) and the *N*-methyl-diamine (IX; R = Me) give cupric salts of type (XI), isolated as the diperchlorates, but that *NNN'*-triethylethylenediamine (X; R = Et) gives solely the bridged dicupric salt (XII).

Irving and Griffiths[10] have determined the stability constants of the cupric and nickel(II) salts of type (XI) formed by the diamines (VII; R = Me and Et) and (VIII; R = Me), and find the salts to be uniformly less stable than the corresponding salts formed from ethylenediamine. Since *N*-alkylation of ethylenediamine in general increases the basic strength of the amine groups, they attribute the weakening of the complex compounds mainly to increasing steric obstruction. A similar conclusion was drawn by Basolo and Murmann,[11] who found that the cupric and nickel salts of type (XI), formed from the diamines (VIII; R = Me, Et, and Pr^n), were less stable than those formed from the corresponding diamines (IX) and from ethylenediamine: it is noteworthy that the diamine (VIII; R = Pr^i) formed cupric salts solely of the bridged type (XII).

$R_2N{\cdot}C_2H_4{\cdot}NH_2$ (VII) $RHN{\cdot}C_2H_4{\cdot}NHR$ (VIII) $RHN{\cdot}C_2H_4{\cdot}NH_2$ (IX) $R_2N{\cdot}C_2H_4{\cdot}NHR$ (X)



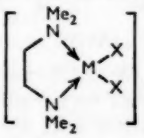
(XI)

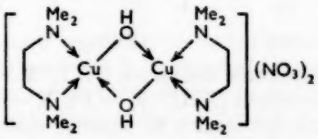


(XII)

In view of the above results, we have been surprised to find that *NNN'N'*-tetramethylethylenediamine, $Me_2N{\cdot}C_2H_4{\cdot}NMe_2$, co-ordinates with palladium dichloride and dibromide, with platinum dichloride, and with iridium dichloride to give stable non-ionic yellow or orange compounds of type (XIII, where M represents the metal and X the co-ordinated halogen atom). These compounds have high melting points and can be readily recrystallised from boiling aqueous solution.

(XIII)





(XIV)

The preparation of the platinous compound (XIII; M = Pt, X = Cl) shows unusual features. When an aqueous solution of the diamine is steadily added to aqueous chloroplatinic acid, the orange chloroplatinate, $C_6H_{16}N_2,H_2PtCl_6$, is first precipitated, but is readily converted by the additional diamine into the pale yellow crystalline compound (XIII; M = Pt, X = Cl). The pure chloroplatinate, when set aside in aqueous suspension for several days, is slowly replaced by the chelated compound, a process which is accelerated if the suspension is boiled. The compound (XIII; M = Pt, X = Cl) can also be prepared less conveniently by the action of the diamine on aqueous sodium chloroplatinite. The preparations from the chloroplatinate clearly involve reduction of the latter with oxidation of the diamine, presumably to its *N*-mono- and di-oxide. We find similarly that the iridium compound (XIII; M = Ir, X = Cl) is best prepared by the action of the diamine on potassium chloroiridate, $K_2[IrCl_6]$, in which the diamine is again acting as a reducing and chelating agent.

This type of compound is not limited to metals giving 4-co-ordinate planar complexes,

[9] Pfeiffer and Glaser, *J. prakt. Chem.*, 1938, **151**, 134.
[10] Irving and Griffiths, *J.*, 1954, 213.
[11] Basolo and Murmann, *J. Amer. Chem. Soc.*, 1954, **76**, 211.

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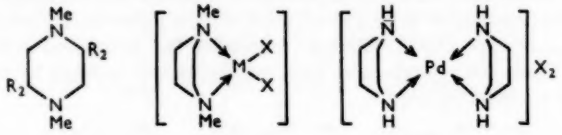
for cadmium chloride gives a similar but colourless compound (XIII; M = Cd, X = Cl), which can be recrystallised from ethanol but decomposes in boiling aqueous solution.

The addition of the diamine (1 equivalent) to an aqueous solution of copper sulphate gave a deep blue solution, which when treated with potassium thiocyanate gave the dithiocyanato-diamine-copper (XIII; M = Cu, X = SCN), and when treated with sodium picrate the dipicrato-diamine-copper (XIII; M = Cu; X = O·$C_6H_2O_6N_3$), both forming very deep green crystals. The last compound has been recrystallised from acetone and identified by analysis and by its molecular weight in boiling acetone. It represents one of the very rare compounds in which the picrate group is directly co-ordinated to a metal.

The addition of the diamine (1·4 equivalents) to copper nitrate in aqueous solution was necessary to redissolve the initial precipitate of cupric hydroxide: the clear solution when concentrated at room temperature gave deep blue crystals of the hydrated bistetramethylethylenediamine-$\mu\mu'$-dihydroxy-dicupric dinitrate (XIV), apparently identical in type with Pfeiffer and Glaser's salt (XII).

Dr. J. Chatt has kindly investigated the conductivities of nitrobenzene solutions of the compounds (XIII; M = Pd, X = Cl; M = Pt, X = Cl; M = Cd, X = Cl; M = Cu, X = ·O·$C_6H_2O_6N_3$); these conductivities are virtually zero, *i.e.*, too small for accurate measurement, and the compounds cannot therefore be salts of the type [(diamine)$_2$M][MX_4]. Further, these compounds are unaffected by the addition of an excess of the diamine to their solutions, and salts of type (XI) cannot be isolated (cf. p. 2778).

Even more surprising is the fact that 1 : 4-dimethylpiperazine (XV; R = H) gives similarly coloured compounds of type (XVI) with palladium dichloride and dibromide, platinum dichloride, and iridium dichloride. These compounds also have high stability, can be recrystallised unchanged from aqueous solution, are unaffected by additional 1 : 4-dimethylpiperazine, and give nitrobenzene solutions of negligible conductivity.



(XV) (XVI) (XVII)

The platinous dichloride derivative (XVI; M = Pt, X = Cl) can be prepared precisely similarly to the compound (XIII; M = Pt, X = Cl), *i.e.*, very readily by the addition of an excess of dimethylpiperazine to aqueous chloroplatinic acid, by spontaneous decomposition of the pure dimethylpiperazine chloroplatinate in aqueous suspension, or by the action of the piperazine on one equivalent of sodium chloroplatinite in aqueous solution. The iridium compound (XVI; M = Ir, X = Cl) has also been prepared by the action of the piperazine on potassium chloroiridate.

It is noteworthy that in compounds of type (XVI) the 1 : 4-dimethylpiperazine is clearly fixed in the boat form. Our attempts to prepare similar chelated metallic derivatives with 1 : 2 : 2 : 4 : 5 : 5-hexamethylpiperazine (XV; R = Me) uniformly failed. This is in harmony with the results of Mann and Senior,[12] who showed that both piperazines readily form dimethobromides and dimethiodides, but whereas 1 : 4-dimethylpiperazine also combines with ethylene dibromide to form triethylenediamine dimethobromide, the hexamethylpiperazine does not undergo a similar reaction. It was suggested that the two sets of *gem.*-dimethyl groups in the piperazine (XV; R = Me) " locked " the molecule in the chair form, which the cation of the crystalline hexamethylpiperazine dinitrate is known to possess.[12] If the molecule of the hexamethylpiperazine in solution is also held rigidly in the chair form, it clearly could not undergo either cyclic diquaternisation with ethylene dibromide or chelation with metals to form compounds of type (XVI).

[12] Mann and Senior, *J.*, 1954, 4476; cf. McElvain and Bannister, *J. Amer. Chem. Soc.*, 1954, **76**, 1126.

The structure of compounds of type (XIII) and (XVI) receives further confirmation from their infrared spectra. Dr. N. Sheppard reports:

" (1) In the spectrum of tetramethylethylenediamine there are medium-to-strong bands at 2800 and 2750 cm.$^{-1}$ and in that of 1 : 4-dimethylpiperazine a similar band at 2810 cm.$^{-1}$. Prominent bands in this region (2800 $\pm$ 50 cm.$^{-1}$) are found consistently when *N*-Me groups occur in free bases, and usually also when *N*-CH_2 groups are present. However, they apparently become shifted to higher frequencies (~2900 cm.$^{-1}$) and are then lost in other CH absorption bands, in the spectra of amine salts in which the nitrogen atom assumes a positive charge.[13]

" In the spectra of the compounds (XIII; M = Pd, X = Cl) and (XVI; M = Pd, X = Cl), the above bands are missing, and this shows clearly that in each compound there are no free *N*-Me groups, *i.e.*, that both tertiary amine nitrogen atoms in each compound are involved in the co-ordination with the palladium atom.

" (2) The infrared spectrum of the liquid 1 : 4-dimethylpiperazine in the ' fingerprint region ' (1400—700 cm.$^{-1}$) is very simple for such a complex molecule. There are indeed fewer absorption bands observable than there are infrared active fundamentals for the most highly symmetrical configuration of the molecule, even in the region below 1200 cm.$^{-1}$ where there is likely to be little overlapping of absorption bands. The spectrum therefore points to the most symmetrical structure for the molecule, *i.e.*, a centro-symmetrical configuration with the 6-membered ring in the ' chair ' conformation, and the *N*-Me groups either both axially (or both equatorially) disposed with respect to the ring.

" In the spectrum of the co-ordinated compound (XVI; M = Pd, X = Cl), the pattern of frequencies changes in many respects, and a number of additional bands of weak or medium strength appear. These changes are consistent with the change in conformation of the dimethylpiperazine molecule from the chair to the boat form caused by chelation with the palladium atom. No extra bands due to the palladium–halogen bonds are likely to be present in the region of the spectrum investigated."

Failure attended attempts to prepare stable co-ordination compounds of tetramethylethylenediamine with Co^{3+}, Rh^{3+}, and Ni^{2+}, and of 1 : 4-dimethylpiperazine with these ions and with Cu^{2+} and Cd^{2+}.

Two major features must be discussed regarding the structure and properties of the two parallel series of compounds (XIII) and (XVI), particularly the palladous, platinous, and iridous members: first, what is the reason for their unexpectedly high stability, both thermal and chemical, and secondly, why is co-ordination limited to one molecule of the diamine to each metallic atom?

There is apparently no intrinsic electronic factor responsible for the stability of these compounds, and their formation is presumably determined almost solely by the marked increase in the co-ordinating power of each tertiary amino-group when both groups are co-operating to form a chelated ring system. This increase in co-ordinating power is evidently much greater than has hitherto been recognised, since it enables two groups, each singly of very weak power, to form a firmly chelating molecule, and it is clearly not necessary (although helpful) for one of the groups to have strong co-ordinating power, as in the compounds (I) and (II).

The reason why only one molecule of tetramethylethylenediamine or 1 : 4-dimethylpiperazine will co-ordinate with one metallic atom is undoubtedly the steric obstruction of the *N*-methyl groups. The evidence for this is two-fold. (i) It is known that palladium and platinum dihalides readily react with ethylenediamine to give salts of type $[M(en)_2]X_2$, and we find that piperazine similarly gives palladium salts of type (XVII). (ii) Figs. 1 and 2 show the positions of a molecule of tetramethylethylenediamine and of dimethylpiperazine respectively when co-ordinated to a palladium atom of ionic radius 1·30 Å. For simplicity, the carbon atom of only one *N*-methyl group is shown attached to the

[13] Nakaniski, Goto, and Ohashi, *Bull. Chem. Soc. Japan*, 1957, **30**, 403.

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upper nitrogen atom in Fig. 1, and no such groups are shown attached to the lower nitrogen atoms in Figs. 1 and 2: circles drawn with thin lines and those with thick lines indicate atoms which are in the plane, and above the plane, of the paper respectively. The following bond lengths have been used: C–C, 1·54; C–H, 1·09; C–N^+, 1·49;[14] Pd–N, 2·02 Å.[15]

In Fig. 1, in order to accommodate the diamine molecule, the normal tetrahedral angles and also the right angle at the palladium atom have been modified by 4—5°, but this should cause a very small degree of strain. The curved dotted line in Fig. 1 indicates the probable extent of the complete methyl group.

It is clear that co-ordination of a second molecule of the diamine in Fig. 1 would bring the four pairs of substituent methyl groups (which would be held rigidly) impossibly close together. It is primarily this steric effect which prevents chelation by a second diamine molecule: a secondary and minor factor is the weaker bonding which would be involved if the palladium atom added further donor atoms, owing to the " ligand " effect.[16]

The same considerations apply to the analogous compounds of Pt^{2+} (1·32 Å) and Cu^{2+} (1·35 Å*) and it is probable that the diamine will co-ordinate stably only with metals

FIG. 1.

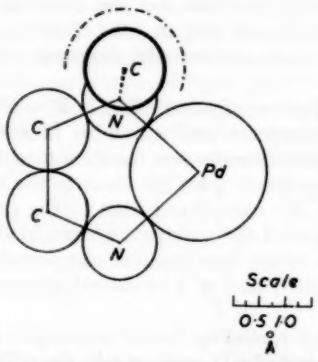
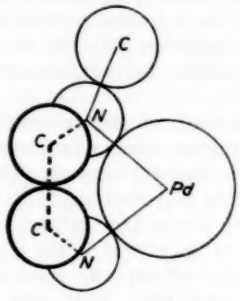


FIG. 2.



Figs. 1 *and* 2 *show the positions of a molecule of tetramethylethylenediamine and of* 1 : 4*-dimethylpiperazine respectively when co-ordinated to a palladium atom. Circles drawn in thin lines and in thick lines indicate atoms which are respectively in and above the plane of the paper. The carbon atom of only one N-*Me *group is shown attached to the upper nitrogen atom in Fig.* 1, *and no such groups are shown attached to the lower nitrogen atoms in Figs.* 1 *and* 2.

having ionic radii in this region. No nickel complexes were isolated, and it is significant that Ni^{2+} has a much smaller ionic radius (0·69 Å). The Cd^{2+} ion (0·97 Å) is tetrahedral, and a similar calculation shows that the bond angles of the diamine are considerably strained in the compound (XIII; M = Cd, X = Cl): it is noteworthy that this compound was the least stable of those of type (XIII).

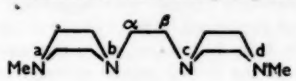
The structure of the dimethylpiperazine–palladium complex (Fig. 2) also shows the great steric obstruction to the chelation of a second molecule of this piperazine. The Figure has been drawn with the carbon angles of 109°, which brings the palladium bond angle very close to 90°: this structure does however reduce the C–N–Pd angle to 90°, but it is probable that the resulting bond strain is shared throughout the ring. Distortion of the more rigid dimethylpiperazine molecule would require more energy than that of the

* This value is based on the Cu–N bond-length of 2·02 Å in $[py_2CuCl_2]$ (Dunitz, *Acta Cryst.*, 1957, **10**, 307) and of 2·07 Å in the cation $[en_2Cu]^{2+}$ (Scouloudi, *ibid.*, 1953, **6**, 651).

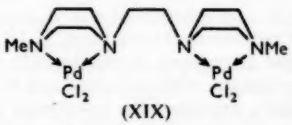
[14] Lister and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 495.
[15] Mann, Wells, and Purdie, *J.*, 1937, 1828.
[16] Cf. Burkin, *Quart. Rev.*, 1951, **5**, 1.

tetramethylethylenediamine molecule: this factor may explain why the piperazine will not co-ordinate stably to the smaller cupric and cadmium ions. No values are apparently available for the ionic radius of Ir^{2+}, but it is undoubtedly very similar to that of Pt^{2+}.

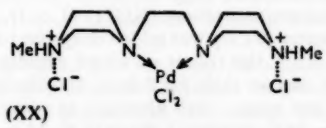
We have briefly investigated the co-ordinating properties of 1 : 2-di-(4-methyl-1-piperazinyl)ethane [17] (XVIII), since this compound consists essentially of two 1 : 4-disubstituted piperazine units linked by an ethylene group, which therefore acts as one of the substituents of each unit. Consideration of the structure of this tetramine indicates that it cannot act as a quadridentate co-ordinating molecule around one central metallic atom, because if, for example, the N^a and N^b atoms in (XVIII) were chelated to a metallic atom, the tetrahedral disposition of the co-ordinated N^b atom would direct the N^b–C^α valency into a position leading so far from the metallic atom that the N^b–C^α–C^β–N^c unit could not then co-ordinate as a chelate group with this atom. Experiment confirms this deduction. The only conditions discovered leading to a fully co-ordinated crystalline palladium derivative entailed treating the tetramine (XVIII) in aqueous solution with two equivalents of potassium chloropalladite, whereby pale yellow crystals of composition $C_{12}H_{26}N_4,2PdCl_2$, undoubtedly tetrachloro-[1 : 2-di-(4-methyl-1-piperazinyl)ethane]dipalladium (XIX), were obtained. The mother-liquor from this preparation, when set aside slowly yielded a crude deposit, which on digestion with hot water afforded deep orange crystals of composition $C_{12}H_{26}N_4,PdCl_2,2HCl,H_2O$. Although there is no evidence for the position of the co-ordinated palladium atom, it is highly probable that this compound is the monohydrated symmetric salt, dichloro-[1 : 2-di-(4-methyl-1-piperazinyl)-ethane 4 : 4'-dihydrochloride]palladium (XX). Unlike the compound (XIX), it is highly soluble in cold water, giving a solution in which only a portion of the chlorine is ionised.



(XVIII)



(XIX)



(XX)

It should be added that Bennett, Mosses, and Statham [18] claim to have prepared dichloro-*NN'*-dimethyl-*NN'*-diphenylethylenediaminepalladium by the interaction of the amine hydrochloride and potassium chloropalladite, but the compound was not further investigated, and its method of preparation, together with its physical properties (" an insoluble buff powder "), suggest that it may have had a much more complex structure.

Experimental

NNN'N'-Tetramethylethylenediamine, b. p. 121°/755 mm., was prepared by the formaldehyde–formic acid methylation of ethylenediamine, 1 : 4-dimethylpiperazine by Mann and Senior's method,[12] and 1 : 2-di-(4-methyl-1-piperazinyl)ethane as described by Mann and Baker.[17]

Metallic Derivatives of NNN'N'-*Tetramethylethylenediamine.*—In the following section this amine will be designated " diamine " for brevity.

Dichloro(diamine)palladium (XIII; M = Pd, X = Cl). The dropwise addition of the diamine (0·23 g.) in water to a stirred aqueous solution of potassium chloropalladite (0·65 g., 1 mol.) precipitated the *compound* (0·58 g., 100%), deep yellow-orange plates, m. p. 245—247° (decomp., darkening at 220°), from water (Found: C, 24·7; H, 5·6; N, 9·3. $C_6H_{16}N_2Cl_2Pd$ requires C, 24·5; H, 5·45; N, 9·5%).

Dibromo(diamine)palladium (XIII; M = Pd, X = Br), similarly prepared, formed deep

[17] Mann and Baker, *J.*, 1957, 1881.
[18] Bennett, Mosses, and Statham, *J.*, 1930, 1668.

XUM

orange prisms, m. p. 226° (decomp.) after crystallisation from much hot water (Found: C, 18·7; H, 4·1; N, 7·2. $C_6H_{16}N_2Br_2Pd$ requires C, 18·8; H, 4·2; N, 7·3%).

These two compounds are sparingly soluble in hot water, very slightly soluble in other polar solvents and insoluble in non-polar solvents. Both crystallised unchanged from a hot aqueous solution containing a large excess of the diamine.

Dichloro(diamine)platinum (XIII; M = Pt; X = Cl). (*a*) The diamine in aqueous solution was added dropwise to pure aqueous chloroplatinic acid which was steadily shaken. The immediate fine precipitate of the orange chloroplatinate was rapidly converted by the additional diamine into the pale yellow *compound* (XIII; M = Pt, X = Cl), m. p. 303° (decomp.) after crystallisation from water (Found: C, 18·8; H, 4·7; N, 7·1. $C_6H_{16}N_2Cl_2Pt$ requires C, 18·8; H, 4·2; N, 7·3%). Addition of a moderate excess of the undiluted diamine to the aqueous acid precipitates this compound without apparent intermediate formation of the chloroplatinate. It is sparingly soluble in hot water and very slightly soluble in boiling ethanol and acetone.

(*b*) The chloroplatinate was precipitated when a solution of the diamine dihydrochloride (0·38 g.) in water (2 c.c.) was added to chloroplatinic acid (1·0 g., 1·2 mols.) in water (2·5 c.c.), and after cooling to 0° was collected, washed with ice-water, and dried. The orange leaflets had m. p. 246° (decomp.), unchanged by recrystallisation from water [(lit.,[19] sinters 245°, m. p. 252° (decomp.)] (Found: C, 13·4; H, 3·3; N, 5·3. Calc. for $C_6H_{16}N_2,H_2PtCl_6$: C, 13·7; H, 3·3; N, 5·3%). A concentrated aqueous solution of this salt, when boiled under reflux for 24 hr., became pale in colour and deposited some platinum. The solution, when filtered and cooled, deposited the above crystalline compound, m. p. and mixed m. p. 303° (decomp.). An aqueous suspension of the finely powdered chloroplatinate, when set aside for many days, gave the same result.

(*c*) Sodium chloroplatinite tetrahydrate and the diamine (1 mol.), each in 10% (w/v) aqueous solution, were mixed. No immediate change was apparent, but the solution when set aside for 5 days became colourless and deposited large crystals contaminated with metallic platinum. Recrystallisation of the deposit from hot water gave the above yellow compound, m. p. and mixed m. p. 303° (decomp.). If the initial mixed solution was heated, a copious deposit of black platinum readily separated.

Dichloro(diamine)iridium (XIII; M = Ir, X = Cl). A solution of the diamine (0·17 g., 3 mols.) in water (2 c.c.) was added dropwise to one of potassium chloroiridate, K_2IrCl_6 (0·24 g.), in water (7 c.c.), the colour of which rapidly changed from deep brown to pale olive-green. The mixture was set aside for 2 days, and the dark precipitate, when collected and recrystallised from much hot water, with filtration to remove iridium, deposited the *compound*, pale yellow prisms, m. p. 288° (decomp.) (Found: C, 19·0; H, 4·5; N, 7·3. $C_6H_{16}N_2Cl_2Ir$ requires C, 19·0; H, 4·25; N, 7·4%). A cold aqueous solution of this compound containing an excess of the diamine was unaffected when set aside for 4 weeks, but on warming rapidly deposited iridium.

The fact that aqueous solutions of potassium chloroiridite, K_3IrCl_6, are olive-green might suggest that the first stage in the above preparation is reduction of the chloroiridate to the chloroiridite: this however is apparently not the case, for we have been unable to prepare the compound (XIII; M = Ir; X = Cl) by the action of the diamine on aqueous solutions of the pure chloroiridite.

Copper derivatives. The diamine (0·46 g., 1 mol.) when added to copper sulphate pentahydrate (0·50 g.), both in aqueous solution, initially deposited cupric hydroxide, which then dissolved to form a very deep blue solution. One portion, diluted with saturated aqueous potassium thiocyanate, deposited *dithiocyanato(diamine)copper* (XIII; M = Cu, X = SCN), very deep green crystals giving an olive-green streak, m. p. 107° after thorough washing with ice-water (Found: C, 32·0; H, 5·7; N, 18·4. $C_8H_{16}N_4S_2Cu$ requires C, 31·6; H, 5·3; N, 18·4%). This compound is soluble in cold acetone and methanol, insoluble in benzene, and very sparingly soluble in cold water, the solution depositing cuprous thiocyanate when warmed.

A second portion of the original solution, when diluted with water and added to sodium picrate solution, deposited *dipicrato(diamine)copper* (XIII; M = Cu; X = ·O·$C_6H_2O_6N_3$), very deep green crystals, black by reflected light, and giving an apple-green streak, m. p. 240° (decomp.) after crystallisation from acetone (Found: C, 34·0; H, 3·3; N, 17·35%; *M*, in boiling acetone, 615. $C_{18}H_{20}O_{14}N_8Cu$ requires C, 34·0; H, 3·15; N, 17·6%; *M*, 636).

A 10% (w/v) aqueous solution (3·3 c.c.) of the diamine (1·4 mols.) was added to a solution

[19] Freund and Michaels, *Ber.*, 1897, **30**, 1385.

of cupric nitrate tetrahydrate (0·48 g.) in water (1·5 c.c.). The clear solution when concentrated at room temperature over sodium hydroxide deposited the *trihydrated bis(diamine)-μμ'-dihydroxy-dicupric dinitrate* (XIV), deep blue crystals, m. p. 178—179° when collected, washed with ice-water and dried in air (Found: C, 25·7; H, 7·5. N, 14·75. $C_{12}H_{34}O_8N_6Cu_2,3H_2O$ requires C, 25·2; H, 7·0; N, 14·7%). These crystals, when confined in a vacuum over sodium hydroxide, effloresced to give the *monohydrate*, a deep royal-blue powder, m. p. 178—179° (Found: C, 27·2; H, 7·0; N, 16·2. $C_{12}H_{34}O_8N_6Cu_2,H_2O$ requires C, 26·9; H, 6·7; N, 16·2%). An aqueous solution of the dinitrate, when either warmed or treated cautiously with dilute nitric acid, gave a copious precipitate of cupric hydroxide.

Dichloro(diamine)cadmium (XIII; M = Cd; X = Cl). Addition of the diamine to aqueous cadmium chloride caused deposition of cadmium hydroxide, which did not dissolve even in a large excess of the diamine. A solution of the diamine (0·47 g., 2 mols.) in ethanol (2 c.c.) was therefore added dropwise to an agitated solution of cadmium chloride (0·46 g.) in ethanol (12 c.c.). The *compound* rapidly separated as colourless silky needles, m. p. 254—255° (in a sealed tube, immersed at 250°), resolidifying to a crystalline mass at 260°, after crystallisation from much ethanol (Found: C, 24·3; H, 5·4; N, 9·6. $C_6H_{16}N_2Cl_2Cd$ requires C, 24·1; H, 5·3; N, 9·35%). It is sparingly soluble in hot ethanol and acetone, and its hot aqueous solution rapidly deposits cadmium hydroxide.

An ethanolic solution, when diluted with an excess of the diamine, boiled under reflux and cooled, deposited the unchanged compound.

Metallic Derivatives of 1 : 4-*Dimethylpiperazine* (XV; R = H).—*Dichloro(dimethylpiperazine)palladium* (XVI; M = Pd; X = Cl). Addition of the piperazine (0·23 g.; 1 mol.) to potassium chloropalladite (0·65 g.), each in aqueous solution, gave a quantitative deposition of the *compound*, deep orange tabular crystals, m. p. 190° (decomp.) after crystallisation from water (Found: C, 24·35; H, 4·6; N, 9·6; Pd, 36·9%; *M*, in boiling water, 294. $C_6H_{14}N_2Cl_2Pd$ requires C, 24·7; H, 4·8; N, 9·6; Pd, 36·8%; *M*, 292).

The *dibromo-compound* (XVI; M = Pd, X = Br), similarly prepared and crystallised, formed deep russet-red prisms, m. p. 172—172·5° (decomp.) (Found: C, 19·3; H, 3·75; N, 7·35. $C_6H_{14}N_2Br_2Pd$ requires C, 18·9; H, 3·7; N, 7·35%).

These two compounds have similar solubilities to those of their tetramethylethylenediamine analogues. Each crystallised unchanged from an aqueous solution containing an excess of the piperazine.

Dichloro(dimethylpiperazine)platinum (XVI; M = Pt, X = Cl). (*a*) An aqueous solution of the piperazine, when added slowly in ultimate excess to chloroplatinic acid solution, first precipitated the orange chloroplatinate, which readily redissolved; the orange solution then deposited the *compound*, pale yellow prisms, m. p. 249° (decomp.; immersed at 240°) from much hot water (Found: C, 19·1; H, 3·5; N, 7·5; Pt, 51·05%; *M*, in boiling water, 350. $C_6H_{14}N_2Cl_2Pt$ requires C, 18·9; H, 3·7; N, 7·4; Pt, 51·3%; *M*, 380). A cold aqueous suspension of the chloroplatinate, $C_6H_{14}N_2,H_2PtCl_6$, behaved similarly when treated with the diamine. The successful preparation of this chloroplatinate [17] depends therefore on the use of an excess of chloroplatinic acid in hydrochloric acid (cf. p. 2778), otherwise the above compound may be formed.

(*b*) An aqueous suspension of the chloroplatinate, when set aside for 21 days, became initially clear and then deposited the above compound, m. p. and mixed m. p. 247° (decomp. as before).

(*c*) The above compound (Found: N, 7·2%) was also prepared from sodium chloroplatinite, as described for the compound (XIII; M = Pt, X = Cl).

Dichloro(dimethylpiperazine)iridium (XVI; M = Ir, X = Cl). This compound was prepared precisely as its tetramethylethylenediamine analogue, and from water formed pale yellow crystals, m. p. 242·5—243·5° (decomp.) (Found: C, 19·2; H, 3·8; N, 7·45. $C_6H_{14}N_2Cl_2Ir$ requires C, 19·1; H, 3·7; N, 7·4%).

Dimethylpiperazine was added to nickel succinimide,[20] both in ethanolic solution, in an unsuccessful attempt to prepare co-ordinated derivatives: the solution, when treated subsequently with an excess of ethanolic sodium iodide, deposited *disodium tetrasuccinimidonickel*, pale mustard-yellow plates, m. p. 328° (decomp.) (Found: C, 38·2; H, 3·7; N, 11·2; Ni, 11·4. $C_{16}H_{16}O_8N_4Na_2Ni$ requires C, 38·5; H, 3·2; N, 11·3; Ni, 11·8%). When sodium succinimide (2 mols.) was added to nickel succinimide, both in ethanolic solution, rapid crystallisation of

[20] Tschugaev, *Ber.*, 1906, **39**, 3197.

Vol. 1958, page 2780, line 6. *For* m. p. 113° (decomp.) *read* m. p. 163° (decomp.).

this salt, m. p. and mixed m. p. 329° (decomp.), occurred. It is insoluble in organic solvents, but readily soluble in water to give a yellow solution which rapidly deposits nickel hydroxide.

Bis(piperazine)palladium dipicrate (XVII; X = ·O·$C_6H_2O_6N_3$). An aqueous solution of piperazine (2 mols.) was added to aqueous potassium chloropalladite, giving immediately a clear pale yellow solution of the dichloride (XVII; X = Cl). This solution, when added to an excess of aqueous sodium picrate, precipitated the *dipicrate*, yellow plates, m. p. 113° (decomp.) (Found: C, 32·6; H, 3·7; N, 18·8. $C_{20}H_{24}O_{14}N_{10}Pd$ requires C, 32·7; H, 3·3; N, 19·1%).

Metallic Derivatives of 1 : 2-*Di*-(4-*methyl*-1-*piperazinyl*)*ethane* (XVIII). (This base will be designated the " tetramine " in this section.)—A solution of the tetramine (0·44 g.) in water (10 c.c.) was added rapidly to a stirred solution of potassium chloropalladite (1·36 g., 2 mols.) in water (20 c.c.), a buff-coloured amorphous precipitate being immediately formed. After 2 min., the mixture was centrifuged, and the upper layer then filtered as rapidly as possible. Almost immediately, there started the slow separation of the pale yellow microcrystalline *tetrachloro(tetramine)dipalladium* (XIX) (0·3 g.) which, when collected after 2 hr., washed with water and acetone, and dried, had m. p. 226° (decomp.) (Found: C, 24·8; H, 4·5; N, 9·5. $C_{12}H_{26}N_4Cl_4Pd_2$ requires C, 24·8; H, 4·5; N, 9·6%): it is insoluble in all the common solvents.

The mother-liquor when set aside for several days continued to deposit the crystals (XIX), contaminated later with minute deep brown needles, probably the tetramine di(chloropalladite), $C_{12}H_{26}N_4,2H_2PdCl_4$. The mixture was collected, and digested with much water at 100° for 2 hr. It was then filtered hot to remove a deep brown sludge, and the filtrate when concentrated and cooled yielded the *monohydrated dichloro(tetramine dihydrochloride)palladium* (XX), hygroscopic deep orange tablets, m. p. 219° (decomp.) after crystallisation from aqueous acetone and drying over silica gel at 20 mm. (Found: C, 28·8; H, 6·2; N, 11·6. $C_{12}H_{26}N_4Cl_2Pd,2HCl,H_2O$ requires C, 29·1; H, 6·1; N, 11·3%). This compound is very soluble in cold water but insoluble in ethanol, acetone, and ether. A dilute aqueous solution, when treated with aqueous silver nitrate, deposits silver chloride but remains orange in colour, showing that the co-ordinated ring system remains intact. The addition of sodium hydroxide to an aqueous solution causes no apparent change.

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566. *An Infrared Absorption Band of the* N-*Methyl Group in the Region of* 2800 *cm.*$^{-1}$.*

By JOHN T. BRAUNHOLTZ, E. A. V. EBSWORTH, FREDERICK G. MANN, and N. SHEPPARD.

The infrared spectra of a variety of organic bases containing the >NMe group include an absorption band of medium to strong intensity between 2760 and 2820 cm.$^{-1}$, which provides a valuable diagnostic test for this group. Structural modifications which involve the lone pair of nitrogen electrons, such as salt formation, or co-ordination of the nitrogen atom to a metal, cause the disappearance of this absorption band; the disappearance is, however, partly masked in the spectra of certain salts by overlapping bands due to >NH^+.

IT has recently been shown[1] that the infrared spectra of compounds containing the methoxyl group include absorption bands of medium strength between 2832 and 2815 cm.$^{-1}$, on the low-frequency side of the alkyl C–H stretching bands. We now draw attention

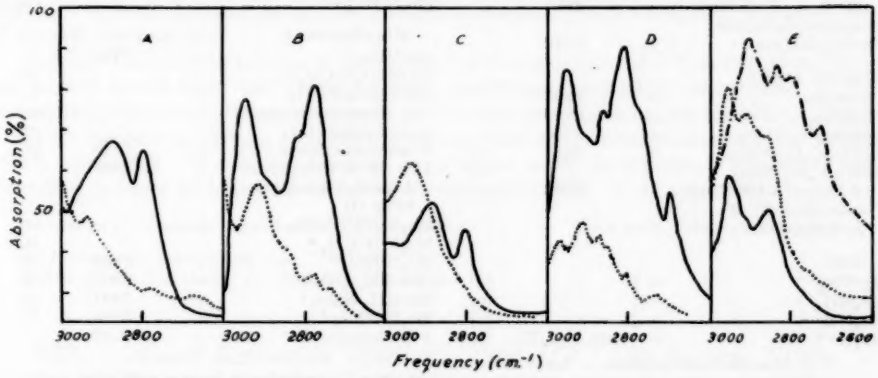
* After the submission of this communication, a paper entitled " Infrared Absorption of NMe and NMe_2 groups in Amines," by Hill and Meakins appeared (*J.*, 1958, 760), in which this characteristic band of the :NMe group when attached to, or contained in, an aromatic, aliphatic, or a non-aromatic heterocyclic system is discussed, without reference however to derivatives in which the lone pair of electrons on the nitrogen atom has become occupied in bond formation.

[1] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462.

to similar features originally observed in recent investigations [2,3] of organic bases containing the >NMe group; their spectra, also, exhibit medium to strong absorption bands, between 2760 and 2820 cm.$^{-1}$, which we believe to be characteristic of the >NMe group, provided that the nitrogen atom retains its lone pair of electrons. The disappearance of this band in the circumstances described below adds to the potential usefulness of the correlation.

Certain typical examples of the *N*-methyl absorption are illustrated in the Figure (*A*—*D*); the Table shows the presence (and, where possible, exact position) or absence of this band in a number of spectra studied by us or recorded elsewhere. We find that the absorption spectrum in the 2800 cm.$^{-1}$ region is sometimes more complex when the nitrogen atom carries an alkyl group other than methyl (Fig. *E*); such cases are not included in the present correlation, although absorption bands very close to 2800 cm.$^{-1}$ have been recorded in the spectra of, for example, diethylamine and triethylamine (Nakanishi *et al.*[4]). However, we consider that the absence of a band of moderate strength in the region of 2800 cm.$^{-1}$ is a reliable criterion for the absence of an >NMe group with a free lone pair of electrons.

Infrared spectra of organic bases and their derivatives in the region 2600—3000 *cm.*$^{-1}$; *substances in liquid film, or in hexachlorobutadiene mull* (*marked* *), *or in vapour phase* (*marked* †).



A, *Dimethylaniline* (——) *and its methiodide* (. . . .).*
B, *Trimethylamine* (——) † *and tetramethylammonium iodide* (. . . .).*
C, *Monomethylaniline* (——) *and N-methylacetanilide* (. . . .).*
D, 1 : 4-*Dimethylpiperazine* (——) *and dibromo*-1 : 4-*dimethylpiperazinepalladium* (. . . .).*
E, *Ethylaniline* (——), *NN-diethyl-p-toluidine* (. . . .), *and piperidine* (— · — · —).

Because of the different physical states of the various samples, the relative intensities of the spectra are not comparable.

There is little doubt regarding the nature of the vibration giving rise to these bands. In the infrared spectrum of monomethylamine vapour, the band at 2820 cm.$^{-1}$ has a parallel-type contour and has accordingly been assigned to the symmetrical C–H stretching frequency of the >NMe group.[5] An earlier assignment of Raman data [6] has suggested that the analogous frequency (2815 cm.$^{-1}$ in the liquid state), and another polarised Raman line at 2880 cm.$^{-1}$, constituted a Fermi-resonance doublet involving the C–H stretching fundamental and the overtone of the symmetrical methyl deformation frequency at 1430 cm.$^{-1}$. This assignment seems slightly preferable, if less specific, but in any case there is no doubt that the intensity of the infrared band is derived principally from the C–H

[2] Mann and Watson, preceding paper.
[3] Braunholtz and Mann, in the press.
[4] Nakanishi, Goto, and Ohashi, *Bull. Chem. Soc. Japan*, 1957, **30**, 403.
[5] Gray and Lord, *J. Chem. Phys.*, 1957, **26**, 690.
[6] Kohlrausch, " Ramanspektren," Becker and Erler, Leipzig, 1943, p. 216.

stretching vibration of the >NMe group. Waldron's infrared data [7] on the methylammonium ion and its *N*-deutero-derivative show that on salt formation the corresponding fundamental C–H stretching vibration has the considerably higher frequency of 2917 cm.$^{-1}$, where it is probably too far removed from the overtone of the CH_3 deformation frequency

The occurrence of a prominent absorption band in the region of 2800 *cm.*$^{-1}$ *in compounds containing* >NMe *groups.* (*Samples in liquid film unless otherwise stated.*)

Compound	Band *	Position †	Phase
Aliphatic amines			
Me·NH_2 [b]	+	2820	(a)
Me_2NH [a]	+		(a)
Me_3N	+	2760, 2810	(a)
Me·NH·NH_2 [a]	+		(a)
$Me_2N·NH_2$ [a]	+		(a)
Me·NH·NHMe [a]	+		(a)
$Me_2N·NHMe$ [a]	+		(a)
$Me_2N·NMe_2$ [a]	+		(a)
$Me_2N·CH_2·CH_2·NMe_2$ [g]	+	2800 (2850, 2750)	(a)
1 : 4-Dimethylpiperazine [g]	+	2810	
1 : 2 : 2 : 4 : 5 : 5-Hexamethylpiperazine	+	2800	
Ph·CH_2·NHMe	+	2780	
Aromatic amines			
Ph·NHMe	+	2807	
Ph·NMe_2	+	2795	
p-Me·C_6H_4·NMe_2	+	2790	
m-NO_2·C_6H_4·NMe_2	+	2815	(c)
p-NO_2·C_6H_4·NMe_2	−		(c)
1 : 2-Dihydro-1-methylquinolino (3′ : 2′-3 : 4)quinoline	+	2790	(c)
Salts			
Me·NH_3^+ [f]	− ‡		(d)
$Me_2NH_2^+$ [b]	− ‡		(c)
Me_3NH^+ [b]	− ‡		(c)
Me_4N^+ [b]	−	see Fig. (B)	(c)
Salts			
$Me_3(n\text{-}C_6H_{13})NH^+$ [a]	−		(b)
Ph·CH_2·$NHMe_2^+$ [a]	−		(b)
Ph·NMe_3^+	−		(c)
Co-ordination compounds			
Dibromotetramethylethylenediaminepalladium [g]	−		(c)
Dibromo-1 : 4-dimethylpiperazinepalladium [g]	−		(c)
trans-$(C_2H_4)PtCl_2·NMe_3$ [e]	−		(c)
Me_3N,BCl_3 [d]	−		(b)
Me_3N,BF_3 [d]	−		(b)
Miscellaneous §			
Me·NO_2	+	2790	
Me·NH·CO·CH_3 [a]	−		(e)
Ph·NMe·CO·CH_3	−		(c)
NN′-Dimethyloxamide [a]	−		(c)
Echinopsine (III)	−		(c)
N-Methylacridone (II)	+	2840	(c)
1 : 2 : 3 : 4-Tetrahydro-1-methyl-4-oxoquinoline (I)	+	2835	
$Me_2N·N{=}N·NMe_2$ [a]	+		(a)
$Me_2N·N{=}CH_2$ [a]	+		(a)
$Me_2N·BCl_3$ [f]	+	2800	(a)
$(Me·SiH_2)_2NMe$ [f]	+	2802	(a)
Me·SiH_2·NMe_2 [f]	+	2801	(a)
$Me_2Si·NMe_2$ [f]	+	2800	(a)
1-Methylpyrrole [g]	+	2812	

* + denotes band present, − band absent.

† Where no position is quoted, the presence of the band was deduced from a published curve or line drawing (*e.g.*, refs. 4 and *a*).

‡ The 2800 cm.$^{-1}$ band is partly overlapped in these spectra by absorption due to >NH^+ groups, but it is nevertheless clear that no prominent bands are present. This is confirmed by the spectra of the >ND^+ derivatives.

§ This section of the Table includes those compounds in which the lone pair may be only partially involved in bond formation.

(a) Gas or vapour. (b) KBr disc. (c) Hexachlorobutadiene mull. (d) Single crystal. (e) CCl_4 solution.

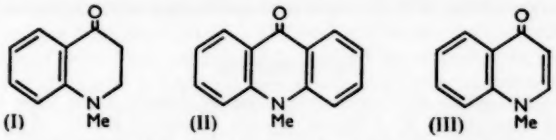
[a] Pierson, Fletcher, and Gantz, *Analyt. Chem.*, 1956, **28**, 1218. [b] Ebsworth and Sheppard, unpublished work. [c] D. B. Powell, personal communication. [d] Peterson and Bauer, personal communication. [e] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1956, **24**, 408. [f] Ebsworth, unpublished work. [g] Mirone and Drusiani, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1954, **16**, 69.

(2 × 1428 cm.$^{-1}$) to interact with it strongly by Fermi resonance. Thus the shift of the >NMe fundamental is the cause of the disappearance of the strong characteristic band on salt formation. Weak overtone bands may still persist in the 2800 cm.$^{-1}$ region.

It is especially noteworthy that medium to strong absorption in the 2800 cm.$^{-1}$ region does not normally occur for molecules in which the nitrogen lone pair of electrons is no longer present as such, *i.e.*, when it is fully involved in bond formation. Thus (see Figure and Table), the absorption band is consistently absent in the spectra of salts (the observations are particularly clear-cut in the case of quaternary compounds: Figs. *A* and *B*),

[7] Waldron, *J. Chem. Phys.*, 1953, **21**, 734.

and when co-ordination of the nitrogen atom to a metal occurs [2] (Fig. *D*). It is also absent (as a prominent band) from the spectra of all the amides studied.



The apparently close correlation between the occurrence or absence of significant >NMe absorption and the degree of commitment of the lone pair is shown by the observations on compounds (I), (II), and (III), which are related to the amides. The band is present at 2835 cm.$^{-1}$ in the normal ketone 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (I); it is weak (at 2840 cm.$^{-1}$) in *N*-methylacridone (II), and absent in the non-ketonic echinopsine (III). There is also an interesting contrast between the compound $Me_2N{\cdot}BCl_2$ (band present) and the closely related compound Me_3N,BCl_3 (band absent). The occurrence of the band in the Si–N–Me derivatives suggests that, although the basic properties of the nitrogen are reduced by the adjacent silicon atom, there remains some degree of localisation of the lone pair on the nitrogen. Hedberg [8] has proposed that in trisilylamine, $(SiH_3)_3N$, coplanar bonding around the nitrogen atom occurs with about 50% delocalisation of the odd electron pair.

Further, the band is present at 2815 cm.$^{-1}$ in the spectrum of *NN*-dimethyl-*m*-nitroaniline, but absent from that of the *p*-isomer, confirming the marked contribution, in the resonance hybrid of the latter compound, of the quinonoid form having the NMe_2^+ group.

From the data at present available, it appears that the *N*-methyl correlation is rather widely applicable. It has, for example, been found useful in structural studies of salt formation in bases such as 1 : 2-dihydro-1-methylquinolino(3′ : 2′-3 : 4)quinoline.[9]

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, February 28th,* 1958.]

[8] Hedberg, *J. Amer. Chem. Soc.*, 1955, **77**, 6491.
[9] Braunholtz and Mann, *J.*, 1955, 381; cf. ref. 3.

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567. *Solvent Extraction Studies. Part II.*[1] *The System Nitric Acid–Water–Tri-*n*-butyl Phosphate.*

By D. G. TUCK.

The extraction of nitric acid from aqueous solution by tri-*n*-butyl phosphate has been investigated. From the volume changes it has been shown that up to ~3·6M-acid in the organic phase the extraction is due to the formation of $Bu_3PO_4.HNO_3$ by addition at the strongly polar P→O group. When this donor oxygen is saturated, further addition takes place at the less basic oxygen atom of a P–O–C bond; in this case, the acid is shown to be extracted as H_2O,HNO_3. The experimental results are discussed in relation to mass-action equations derived for these two types of equilibrium.

IN Part I [1] it was shown that the species extracted from aqueous nitric acid by an organic solvent could be identified by a quasi-dilatometric method in which changes in the volumes of the two phases were measured. In the work described below, this technique has been used as the starting point for an investigation of the interaction of aqueous nitric acid with the solvent tri-*n*-butyl phosphate. Some of the features of this system have already been discussed by Alcock, Grimley, Healy, Kennedy, and McKay.[2] The present work has removed some of the anomalies in their treatment and revealed factors not discussed

[1] Part I, Tuck, *J.*, 1957, 3202.
[2] Alcock, Grimley, Healy, Kennedy, and McKay, *Trans. Faraday Soc.*, 1956, **52**, 39.

by them. As these authors emphasise, tri-*n*-butyl phosphate is a good extractant for many inorganic nitrates, and a full understanding of its reactions with nitric acid is essential for a complete interpretation of its behaviour in multicomponent systems.

Experimental

Reagents.—Analytical-grade nitric acid was suitably diluted some time before use; acid concentrations were determined by titration against standard alkali. Aliquot parts of the organic phase were dissolved in an excess of aqueous acetone before titration.

A solution of potassium nitrate was made up from " AnalaR " material.

Commercial tri-*n*-butyl phosphate (100 ml.) was refluxed with 0·5% aqueous sodium hydroxide (500 ml.) for 10 min. and the mixture then distilled in a slow stream of air, to prevent excessive " bumping; " this distillation was continued until about 200 ml. had been collected. The remaining material was washed at least six times with its own volume of water. Excess of water was removed by addition of anhydrous magnesium sulphate and filtration under suction. Infrared spectroscopy showed that the final product contained no dibutyl hydrogen phosphate.

Extraction Measurements.—Determinations of acidity in the organic phase, extraction coefficient, and volume change arising from extraction of nitric acid followed those outlined in Part I. Since tri-*n*-butyl phosphate has a relatively high specific gravity, mixtures of the solvent and weak aqueous solutions of nitric acid took a considerable time to settle after mixing. All solutions were centrifuged to ensure complete separation of the phases before determination of the nitric acid concentration in each. In the present experiments, no detectable change in the total volume of the system occurred as a result of the extraction.

For measurements of the extraction of nitric acid from aqueous nitric acid–potassium nitrate mixtures, equal volumes of the two phases were stirred together for 10 min., then centrifuged.

Infrared Spectra.—The infrared absorption spectra of certain solutions of nitric acid in tri-*n*-butyl phosphate were examined, as liquid films, in a Perkin-Elmer double-beam spectrometer.

Density Measurements.—The density of solutions of nitric acid in the organic phase was determined by weighing, by difference, the amount of solution contained in a graduated micropipette (capacity ~0·5 ml.). After being weighed, the solution was quantitatively removed from the pipette and the acid concentration determined as described earlier.

Results and Discussion

Volume Changes.—Fig. 1 shows the change in volume of the organic phase plotted against the amount of nitric acid extracted. Since it has been shown that tri-*n*-butyl phosphate is essentially insoluble in aqueous nitric acid,[2] these changes lead directly to the identification of the extracted species.

It should first be noted that the value of ΔV for the transfer of water only (*i.e.*, zero nitric acid concentration) is in good agreement with the postulated formation of a Bu_3PO_4,H_2O complex.[2,3] Five ml. of tri-*n*-butyl phosphate[4] (*d* 0·973) contain 18·3 mmoles, so one should find a volume change of 0·329 ml. (18·3 mmoles of water) on saturation; the solubility of tri-*n*-butyl phosphate in water is negligible compared with that of water in the ester. The experimental result ($\Delta V = 0{\cdot}31$ ml.) is in good agreement with this argument, within the limits of the measurements in this region where, as noted previously, the very similar densities of the two phases cause some difficulty.

It is clear from Fig. 1 that two distinct types of interaction are responsible for the extraction of nitric acid, and that the region in which both can occur simultaneously is small. Extrapolation of the two straight portions of the curve shows that the point of intersection is at 18·7 mmoles of nitric acid extracted, equivalent to the complete formation of a complex Bu_3PO_4,HNO_3. Below this point it is suggested that effectively

[3] Moore, AECD–3196.
[4] Scheflan and Roberts, " Handbook of Solvents," MacMillan and Co. Ltd., London, 1953, p. 658.

all the tri-*n*-butyl phosphate is present as either Bu_3PO_4,H_2O or Bu_3PO_4,HNO_3. In terms of the change in volume of the organic phase in relation to increasing extraction of nitric acid, this implies the replacement of water in the organic phase by nitric acid, with an overall volume change of (41·5 — 18·0) ml. per mole of nitric acid extracted. The experimental slope of 0·0237 ml. per mmole is in good agreement. In the region of higher acidity, the slope of the curve is 0·055 ml. per mmole of nitric acid extracted, or 18·2 mmoles per ml. This is almost identical with the value found previously [1] for the extraction of nitric acid into diethylene glycol dibutyl ether, where the extracted species was shown to be H_2O,HNO_3.

These results suggest the following scheme for the interaction of tri-*n*-butyl phosphate with aqueous nitric acid. At low acidities, up to about 7M (equilibrium) aqueous nitric

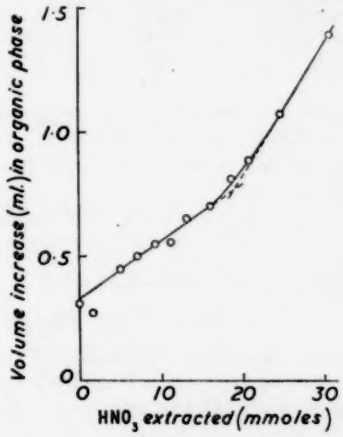


FIG. 1. *Volume changes in tri-n-butyl phosphate due to the extraction of nitric acid.*

acid, the extraction is entirely due to the strongly polar P→O group, which can form a complex directly with a nitric acid molecule. When all the tri-*n*-butyl phosphate is in the form of Bu_3PO_4,HNO_3, further addition takes place on the weakly basic oxygen atom of one of the butoxy-groups. The argument implies that there are no hydrated nitric acid complexes of the type Bu_3PO_4,HNO_3,H_2O postulated by McKay and his group. Their results on the water content of tributyl phosphate solutions of nitric acid are in qualitative agreement with the present theory, showing a fall in water content with increasing nitric acid concentration up to an $HNO_3 : Bu_3PO_4$ ratio of about 1, followed by an increase above this value. However, in the low acidity region, they find that the sum of the water and the nitric acid concentration is greater than the available moles of solvent. This may be due to take-up of some water by a butoxy-oxygen atom, although this is difficult to reconcile with the good straight line found in the present work for the volume change.

Partition Data.—The experimental results for nitric acid partitions up to an aqueous phase equilibrium concentration of 14M are given in Table 1. There is a maximum value of E_{HNO_3} at ~M-nitric acid (aqueous phase); at higher concentrations the extraction coefficient reaches a fairly constant value of approximately 0·35. The latter change occurs at ~3·4M-nitric acid in the organic phase, corresponding to saturation of the P→O group and the beginning of addition at a butoxy-group, as suggested above.

It has been shown [2] that for dilute (2%) solutions of tri-*n*-butyl phosphate in an inert solvent, the law governing the partition is:

$$[Bu_3PO_4,HNO_3]/[Bu_3PO_4(f)] \,.\, a_{HNO_3} = \text{Constant}$$

where a_{HNO_3} is the activity of nitric acid in the equilibrium aqueous phase; $Bu_3PO_4(f)]$ and $[Bu_3PO_4,HNO_3]$ are the concentrations of uncomplexed ester and of nitric acid in the organic phase. It appears, however, from McKay's paper (ref. 2, fig. 4) that this is far from valid for 100% ester. Further, deviations are appreciable for all concentrations of ester in the organic phase once the HNO_3 : ester ratio exceeds unity; this point will be discussed below. The importance of extraction of water in the low acidity region

TABLE 1. *Partition of nitric acid between tri-*n*-butyl phosphate and aqueous solution.*

Aqueous phase HNO_3 concn. (M)	Organic phase HNO_3 concn. (M)	E_{HNO_3}	Aqueous phase HNO_3 concn. (M)	Organic phase HNO_3 concn. (M)	E_{HNO_3}
0·098	0·031	0·32	2·41	1·68	0·699
0·150	0·069	0·47	3·21	2·00	0·624
0·270	0·175	0·66	4·12	2·31	0·560
0·41	0·33	0·81	5·75	2·83	0·493
0·535	0·46	0·86	7·49	3·21	0·429
0·765	0·685	0·895	9·69	3·50	0·362
1·10	0·93	0·845	11·55	4·06	0·353
1·70	1·32	0·778	13·73	4·84	0·352

has been emphasised earlier, suggesting that any law governing the system 100% Bu_3PO_4–HNO_3–H_2O must take account of this. Two mass-action equations of the type quoted above can be set up for the formation of the Bu_3PO_4,H_2O and Bu_3PO_4,HNO_3 complexes:

$$K_1 = [Bu_3PO_4,H_2O]/Bu_3PO_4(f)] \,.\, a_{H_2O}$$

$$K_2 = [Bu_3PO_4,HNO_3]/[Bu_3PO_4(f)] \,.\, a_{HNO_3}$$

Combining these, one should have:

$$[Bu_3PO_4,H_2O]/[Bu_3PO_4,HNO_3] = K_1 \,.\, a_{H_2O}/K_2 \,.\, a_{HNO_3} \quad . \quad . \quad . \quad (1)$$

where the activities are again those in the equilibrum aqueous phase. Complex formation in this low-acid region is concerned exclusively with the polar P→O group so that, in testing equation (1), the amount of water has been calculated as:

$$\text{mmoles of } H_2O = \text{mmoles of ester(p)} - \text{mmoles of } HNO_3\text{(org)}$$

where ester(p) implies pure tri-*n*-butyl phosphate (*i.e.*, 18·3 mmoles per 5 ml.). This is based on the volume changes discussed above; it does not exclude presence of additional water in the organic phase, but implies rather that any such water, which must be small in quantity, is not concerned in the extraction mechanism in this concentration region. The results of these simple calculations are given in Table 2, along with the relevant values [5] of a_{HNO_3} and a_{H_2O}.

TABLE 2. *Water in tri-*n*-butyl phosphate solutions of nitric acid.*

HNO_3, mmoles (expt.)	H_2O, mmoles (by subtraction)	a_{HNO_3}	a_{H_2O}	HNO_3, mmoles (expt.)	H_2O, mmoles (by subtraction)	a_{HNO_3}	a_{H_2O}
0·163	18·1$_5$	0·006	0·997	5·02	13·3	0·685	0·965
0·368	17·9	0·015	0·995	7·13	11·2	1·89	0·943
0·935	17·3$_5$	0·040	0·991	9·32	9·0	4·71	0·914
1·71	16·6	0·091	0·987	11·20	7·1	10·9	0·873
2·46	15·8	0·152	0·983	13·1	5·2	24·5	0·818
3·70	14·6	0·312	0·974	16·1	2·2	76·4	0·710

Equation (1) has been tested against the data in Table 2 by plotting a_{HNO_3} (*i.e.*, $m_\pm^2\gamma_\pm^2$) against $a_{H_2O}[Bu_3PO_4,HNO_3]/[Bu_3PO_4,H_2O]$. The resultant curve (Fig. 2) shows that below about 0·4M (aqueous) nitric acid equation (1) is indeed valid. The limiting slope of 1 on this log–log plot is in agreement with the low degrees of dissociation estimated by McKay and his co-workers [2] on the basis of the semi-empirical relation proposed by Walden,[6] and with conductivity measurements.[7]

[5] Data from Landolt–Börnstein's " Tabellen."
[6] Walden, " Acids, Bases and Salts," McGraw-Hill, New York, 1929, pp. 283 *et seq.*
[7] Healy and McKay, *Trans. Faraday Soc.*, 1956, **52**, 633.

Above this region of linearity one finds lower values of the term

$$a_{H_2O}[Bu_3PO_4,HNO_3]/[Bu_3PO_4,H_2O]$$

than would be predicted from the nitric acid activity in the equilibrium aqueous phase. A tentative explanation is the following. In writing the mass-action equations on which equation (1) is based, it has been assumed that the activity coefficients for the species Bu_3PO_4,HNO_3 and Bu_3PO_4,H_2O can be neglected. This is probably quite justified for the former in the absence of dissociation, since attractive interactions appear unlikely; this supposition is certainly confirmed for nitric acid species in dibutylcarbitol,[1] and in the high acidity region of the present system, where the results are explained satisfactorily

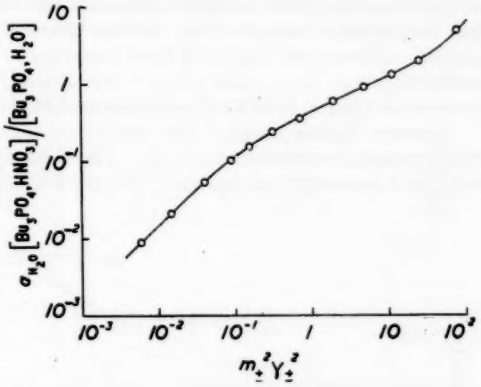


FIG. 2. *Nitric acid extraction into tri-n-butyl phosphate as a function of aqueous nitric acid activity.*

without the introduction of activity coefficients for the organic phase. For Bu_3PO_4,H_2O, however, one can envisage the formation of weak association complexes, reducing the activity of the monomeric species. Re-writing equation (1) in the form plotted in Fig. 2, one has

$$a_{H_2O}[Bu_3PO_4,HNO_3]/f_1[Bu_3PO_4,H_2O] = \text{Constant} \times a_{HNO_3}$$

where f_1 is the activity coefficient for Bu_3PO_4,H_2O. At sufficiently low nitric acid concentrations in the organic phase, the amount of Bu_3PO_4,H_2O is effectively constant and few of the postulated Bu_3PO_4,H_2O dimers would be affected by changes in the amount of nitric acid extracted. Under these conditions, f_1 would be constant. With increasing replacement of Bu_3PO_4,H_2O by Bu_3PO_4,HNO_3, the possibility of dimer formation is reduced and so the activity coefficient of the monomer rises, leading to the type of change observed. For an organic phase such as 2% of ester in kerosene, in which water is essentially insoluble, consideration of the behaviour of water in the organic phase is unnecessary. Under these conditions, equation (1) reduces to the form proposed by McKay *et al.*[2], which is a limiting case of the more general equation. Organic phases of intermediate composition will behave as the appropriate mean of these two sets of conditions.

Alternatively, or additionally, one might suppose that deviations from ideality are due to attractive interactions between Bu_3PO_4,H_2O and Bu_3PO_4,HNO_3. Again, such interactions would have little effect at low nitric acid concentrations or in systems of negligibly small water content. It is hoped to investigate this problem later.

When the nitric acid concentration in tri-*n*-butyl phosphate is such that the donor activity of the P→O group is approaching saturation, the slope of the curve in Fig. 2 begins to rise and one might believe that the slope is again approaching unity. The situation is complicated, however, at these acidities by the onset of extraction of nitric

acid by addition at a butoxy-group, as shown by the results in Fig. 1, so that it is difficult to ascribe any significance to this change of slope.

Infrared Spectra.—Although the results show that the Bu_3PO_4,HNO_3 complex is not dissociated into free ions to any extent, the highly polar nature of tri-*n*-butyl phosphate should produce significant ion-pair formation. The infrared spectra are in agreement with this; the spectrum of a solution of the approximate composition Bu_3PO_4,HNO_3 shows absorption bands at 1400 and 810 cm.$^{-1}$, characteristic of ionic organic nitrates.[8] One also finds a broad band with a maximum at about 2550 cm.$^{-1}$, arising from a hydrogen-bonded P→O group.[9] These results suggest that the complex is actually $(BuO)_3P{\rightarrow}O \cdots H^+,NO_3^-$.

The System Bu_3PO_4–*Aqueous* $HNO_3 + KNO_3$.—The extraction of nitric acid by tri-*n*-butyl phosphate from aqueous solutions containing both nitric acid and potassium nitrate has been briefly studied. This salt was chosen because of its low solubility in the organic phase.[7] The results (Table 3) show a marked " salting out "; unfortunately the activity coefficients a_{H^+}, $a_{NO_3^-}$, and a_{H_2O} are not available for mixed solutions of nitric acid and potassium nitrate, so that a complete analysis of the results is not possible.

Density Measurements.—The density of a series of solutions of nitric acid in tri-*n*-butyl phosphate is shown in Fig. 3. The value for zero nitric acid is in fact that for water-saturated tri-*n*-butyl phosphate. For the low-acidity region, Fig. 3 shows a smooth curve,

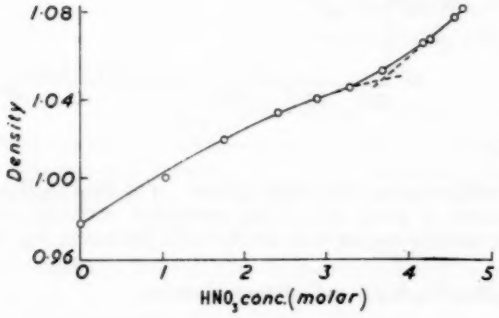


FIG. 3. *Density of solutions of nitric acid in tri-n-butyl phosphate.*

in general agreement with the theory advanced above of non-ideal behaviour. In the high-acidity region, there is a linear increase of density, d, with increasing nitric acid concentration, given by $d = \text{Constant} + 0{\cdot}034c$, where c is the molar concentration of nitric acid. This slope can be compared with the value 0·0338 found for solutions of nitric acid monohydrate in diethylene glycol dibutyl ether.[1] The point at which the two

TABLE 3. *Extraction of nitric acid by tri-n-butyl phosphate from aqueous solutions of* $HNO_3 + KNO_3$.

Original aq. HNO_3 concn. (M)	0·60	0·60	0·60	0·60	0·60	0·60
Original aq. KNO_3 concn. (M)	0	0·30	0·45	0·60	0·90	1·20
Final organic phase HNO_3 concn. (M) ...	0·274	0·315	0·330	0·342	0·360	0·382

portions of the curve intercept on extension corresponds to a $Bu_3PO_4 : HNO_3$ ratio of unity, equivalent to complete formation of Bu_3PO_4,HNO_3.

High-acidity Region.—From the evidence of the volume changes and of the density relation, it is clear that in the high-acidity region one is observing the addition of

[8] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen, London, 1954, p. 255.
[9] Bellamy, *loc. cit.*, p. 257.

H_2O,HNO_3 to the weakly basic oxygen of a butoxy-group. This should then obey the equation

$$Bu_3PO_4,HNO_3 + HNO_{3(aq.)} \rightleftharpoons Bu_3PO_4,HNO_3(H_2O,HNO_3)$$

in which case there should be a relation of the type:

$$\frac{[\text{Nitric acid in ester as } H_2O,HNO_3]}{[\text{"Free" } Bu_3PO_4,HNO_3]} \propto a_{HNO_3} \quad . \quad . \quad . \quad . \quad (2)$$

The total amount of nitric acid present in the organic phase as H_2O,HNO_3 is given by (total HNO_3 — 18·3) and that of "free" Bu_3PO_4,HNO_3 by [18·3 — (H_2O,HNO_3)]. A rough quantitative test of equation (2) has been made by using the two results at highest nitric concentration (Table 1); Fig. 1 shows that only at these concentrations is the species extracted uniquely H_2O,HNO_3.

TABLE 4. *Extraction of nitric acid by* Bu_3PO_4,HNO_3.

Total HNO_3 in ester phase (mmoles)	HNO_3 as H_2O,HNO_3 (mmoles)	"Free" Bu_3PO_4,HNO_3 (mmoles)	Ratio	HNO_3 concn., aq. phase (M)	$m_\pm^2\gamma_\pm^3$
24·8	6·5	11·8	0·55	11·55	1430
30·9	12·6	5·7	2·21	13·73	3550

These values agree with the writing of equation (2) as

$$\left[\frac{\text{Nitric acid in ester as } H_2O,HNO_3}{\text{"Free" } Bu_3PO_4,HNO_3}\right] = 8{\cdot}0 \times 10^{-4}(m_\pm^2\gamma_\pm^2 - 700)$$

where the term in the square bracket is the mole ratio. The value of 700 found for the constant by graphical extrapolation is the value of $m_\pm^2\gamma_\pm^2$ for zero extraction of nitric acid as H_2O,HNO_3; this corresponds to an equilibrium aqueous phase of 9·9M-nitric acid, which would be in equilibrium with an organic phase of 3·5M-nitric acid. This is again in agreement with the scheme proposed above, according to which addition of H_2O,HNO_3 does not begin until the Bu_3PO_4,HNO_3 complex is completely formed. The exactness of this agreement is perhaps fortuitous, since there is some uncertainty in the interpolation of the activities in this concentration region.

There remains the difference in the interaction of nitric acid with the two different donor groups of tri-*n*-butyl phosphate. It appears that the strong polarity of the P→O bond allows this oxygen atom to solvate a hydrogen ion (or atom) directly, but that the less basic ester-oxygen is unable to do this and so can only form a hydrogen bond with (effectively) H_3O^+. Another interesting consequence of the strongly basic nature of the P→O bond is that tri-*n*-butyl phosphate extracts hydrochloric acid from aqueous solution, whereas ethereal or ketonic solvents extract this acid only slightly.[10]

Dr. G. D. Meakins, Dr. J. G. Watkinson, and Professor R. M. Diamond (Cornell University, Ithaca, New York) are thanked for useful discussions.

DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MANCHESTER, MANCHESTER, 13. [*Received, October 28th*, 1957.]

[10] Tuck, unpublished results.

568. *Cyclic Organic Boron Compounds. Part I. Preparation, Characterisation, and Stability of Esters of Metaboric Acid.*

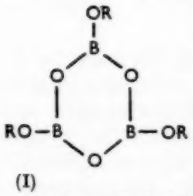
By M. F. Lappert.

The lower alkyl (Me, Et, Pr^n, Pr^i, Bu^n, Bu^i, and Bu^s, but not Bu^t) metaborates, $(RO{\cdot}BO)_3$, have been prepared by thermal or catalytic decomposition of corresponding dialkyl chloroboronates, $(RO)_2BCl$, or by heating the orthoborates with boron trioxide. The last method was also successful for phenyl metaborate. Infrared spectra showed strong absorption bands near 720 and 735 cm.$^{-1}$ which appear to be diagnostic for metaborates. The esters, although thermally very stable, disproportionated when strongly heated under reduced pressure, and were also readily hydrolysed.

This paper * is the first in a series dealing with the chemistry of cyclic organic boron compounds, and in particular with six-membered ring compounds having alternate boron atoms and atoms capable of " back-co-ordinating " to boron.

Until recently the existence of alkyl metaborates, RO·BO, had not definitely been established,[1] although the orthoborates, $(RO)_3B$, have been known since 1846 [2] and numerous detailed investigations have been reported concerning their preparation, structure, and chemical and physical behaviour.[1] By contrast, in inorganic chemistry, the meta- (or 1 : 1)borates are better known than the ortho(or 3 : 1)borates.[3]

Goubeau and Keller obtained methyl metaborate by heating the orthoborate and boron trioxide in equimolecular proportions in a sealed tube.[4] It was trimeric and this, taken in conjunction with its Raman spectrum,[5] was evidence for a formulation (I; R = Me). Trimeric (−)-menthyl and *cyclo*hexyl metaborate, prepared by azeotropic removal (with toluene) of water from an equimolecular mixture of orthoboric acid and the appropriate alcohol, were considered to have no characteristic infrared B=O absorption and were also formulated as (I) [6]; this view of the spectra was taken because all the bands in the 2—9 μ region were attributed to CH absorption. Alkyl metaborates have also been postulated as intermediates in the decomposition of dialkyl chloroboronates, $(RO)_2B{\cdot}Cl$, producing alkyl chloride, this being markedly catalysed by traces of Lewis acids.[7]



(I)

The alkyl metaborates were obtained by reaction (1) $3(RO)_2B{\cdot}Cl \longrightarrow (RO{\cdot}BO)_3 + 3RCl$ or (2) $(RO)_3B + B_2O_3 \longrightarrow (RO{\cdot}BO)_3$; attempted preparation of the *n*-butyl homologue by hydrolysis of the orthoborate with a limited amount of water failed, orthoboric acid being precipitated. Reaction (1) was carried out (*a*) at 150—250°, under pressure if necessary, depending on the boiling point of the reactant, or (*b*) without heat, by the addition of a trace of anhydrous ferric or aluminium chloride. Reaction (2) was carried out by heating the mixture under reflux, or under pressure if necessary, until the trioxide had dissolved (a slight excess of boron trioxide is recommended).

Neither of the methods was suitable for the preparation of *tert.*-butyl metaborate; di-*tert.*-butyl chloroboronate does not exist [7] and reaction of the orthoborate with boron trichloride produced mainly boron trioxide. Reaction (1) is not suitable for aryl metaborates, in view of the different mode of decomposition of diaryl chloroboronates.[8]

Some physical constants of the metaborates are shown in Table 1, including molecular

* Partly covered by B.P. Application 22444/57.

[1] Lappert, *Chem. Rev.*, 1956, **56**, 959.
[2] Ebelmen and Bouquet, *Ann. Chim. Phys.*, 1846, **3**, 17, 54; *Annalen*, 1846, **60**, 251.
[3] Kemp, " The Chemistry of Borates," Part I, Borax Consolidated Ltd., London, 1956.
[4] Goubeau and Keller, *Z. anorg. Chem.*, 1951, **267**, 1.
[5] *Idem, ibid.*, 1953, **272**, 303.
[6] O'Connor and Nace, *J. Amer. Chem. Soc.*, 1955, **77**, 1578.
[7] Lappert, *J.*, 1956, 1768.
[8] Colclough, Gerrard, and Lappert, *J.*, 1955, 907; 1956, 3006.

TABLE 1.

R in $(RO{\cdot}BO)_3$	n_D^{20}	d_4^{20}	M. p.	$[R_L]_D$ Found	$[R_L]_D$ Calc.
Me	1·4038	1·233	—	34·4	34·1
Et	1·4071	1·113	—	47·7	48·0
Pr^n	1·4129	1·025	—	62·6	62·0
Pr^i	—	—	52—54°	—	—
Bu^n	1·4236	1·014	—	75·3	75·9
Bu^i	1·4170	0·997	—	75·8	75·9
Bu^s	1·4151	0·985	—	76·1	75·9
Ph	—	—	98—101	—	—

refractivities calculated from the measured refractive indices and densities which are in reasonable agreement with the values calculated from accepted atomic and structural constants [9] and a value of 2·20 for the atomic refractivity of boron (this is substantially lower than the 2·65 for boron in orthoborates [7]). The three isomeric butyl metaborates were shown to be trimeric, their formulæ thus being (I). The metaborates were soluble in many organic solvents, including diethyl ether, benzene, *n*-pentane, and methylene dichloride.

Strong bands between 1500 and 1300 cm.$^{-1}$ in the infrared spectrum of methyl metaborate are undoubtedly due to the modes involving B–O stretching and mask the methyl deformation bands. A band at 1486 cm.$^{-1}$ with a shoulder at 1520 cm.$^{-1}$ is at a considerably higher frequency than is usual [10,11] for B–O single-bond stretching frequencies, suggesting bonds of higher order. The spectra of the higher alkyl metaborates contain more bands in the regions 1300—1500 cm.$^{-1}$ than does the spectrum of methyl metaborate owing, probably, to the wider occurrence of rotational isomers as the alkyl group becomes larger. It seems that *cyclo*hexyl and menthyl metaborate [6] should have similar absorptions in this region of the spectrum which, of course, is within the range 2—9 μ. All the alkyl metaborates absorb strongly in the region 1050—1100 cm.$^{-1}$ (C–O bond stretching). In phenyl metaborate the corresponding bands occur at 1225 and 1209 cm.$^{-1}$ as expected for ether links. Further strong absorption which appears highly characteristic for metaborates occurs near 720 and 735 cm.$^{-1}$, the intensities being of the same order as those of the C–O bands near 1100 cm.$^{-1}$. Such bands do not occur in the spectra of trialkyl orthoborates [10] and it is possible that they arise from the out-of-plane vibrations of the B_3O_6 skeleton. However, whatever the cause of these bands, strong absorption near 720 and 735 cm.$^{-1}$ is of good diagnostic value for metaboric esters.

Attempted distillation under reduced pressure of the metaborates caused disproportionation [reverse of reaction (2)]; in order to distil the orthoborate, a bath temperature substantially higher than its boiling temperature had to be employed. This result explains the stoicheiometry proposed previously for decomposition of dialkyl chloroboronates.[7] When heated at high temperature under reflux, on the other hand, the metaborates were stable; for example the *n*-butyl homologue showed no significant decomposition after 5 hours at 280—290° (cf. ref. 6).

The metaborates, like most orthoborates,[1] were hydrolysed readily by cold water, to boric acid and the alcohol or phenol.

EXPERIMENTAL

Preparations, Boron Analysis, and Hydrolysis.—The orthoborates (Me,[12] Et,[13], Bu^t,[14] Ph,[8] and the others [15]) and dialkyl chloroboronates (Me and Et,[16] and the others [7]) were prepared

[9] Vogel, *J.*, 1946, 133; 1948, 616, 644, 654.
[10] Webster and O'Brien, *Austral. J. Chem.*, 1955, **8**, 355; 1956, **9**, 137.
[11] Dandegaonker, Gerrard, and Lappert, *J.*, 1957, 2872; Abel, Gerrard, and Lappert, *J.*, 1957, 3833.
[12] Vaughn, U.S.P. 2,088,935/1937.
[13] Wiberg and Sütterlin, *Z. anorg. Chem.*, 1931, **202**, 1.
[14] Brown, Mead, and Shaaf, *J. Amer. Chem. Soc.*, 1956, **78**, 3613.
[15] Scattergood, Miller, and Gammon, *ibid.*, 1945, **67**, 2150.
[16] Wiberg and Smedsrud, *Z. anorg. Chem.*, 1935, **225**, 204.

by established methods. Boron in phenyl metaborate,[17] the alkyl metaborates,[7] and boron trioxide was estimated by procedures described previously. All the metaborates were readily hydrolysed by cold water; this was shown analytically. M. p.s were determined in sealed capillary tubes.

Preparation (1) *of Alkyl Metaborates.*—Details of these experiments are shown in Tables 2 and 3; the general procedure was to decompose the dialkyl chloroboronate (4—30 g.) either under reflux for a stated time or by adding a catalyst. The metaborate was separated from the alkyl chloride by filtration (Pr^i) or evaporation of the chloride under reduced pressure. When a catalyst was used, this was removed by dissolving the metaborate in an inert anhydrous solvent, such as methylene dichloride or diethyl ether and filtering the whole. The solvent was removed from the filtrate under reduced pressure.

Preparation (2) *of Alkyl and Phenyl Metaborates.*—A mixture of the orthoborate (1 mol.) and boron trioxide (slightly >1 mol.) was heated under stated conditions as shown in Table 4. Purification of the metaborate was effected by dissolving the product in a large volume of an inert anhydrous solvent, filtering, and evaporating the filtrate under reduced pressure.

Unsuccessful Attempts to prepare Metaborates.—(*a*) *tert.*-Butyl orthoborate (6·25 g.) and

TABLE 2.

R in $(RO{\cdot}BO)_3$	Time (hr.)	Temp.	Catalyst (% w/w)	Yield (%)	Yield * (%) of RCl
Me	10	250° (sealed)	—	99	—
Et	10	250° (sealed)	—	100	—
Pr^n	10	250° (sealed)	—	99	80
Pr^i	5	200° (sealed)	—	98	76
Bu^n	10	250° (sealed)	—	100	85
Bu^n †	3	20°	$FeCl_3$ (0·28)	93	—
Bu^i	10	250° (sealed)	—	99	83
Bu^s	3	20°	$AlCl_3$ (0·16)	96	—

* RCl characterised by n_D^{20}. † $(RO{\cdot}BO)_3$ had n_D^{20} 1·4235 (Found: B, 10·8%).

TABLE 3.

R in $(RO{\cdot}BO)_3$	n_D^{20}	Found (%) C	Found (%) H	Found (%) B	Required (%) C	Required (%) H	Required (%) B
Me	1·4060	20·6	4·97	19·4	20·7	5·23	18·7
Et	1·4083	32·9	6·84	15·4	33·3	6·95	15·0
Pr^n	1·4143	42·8	8·1	12·4	42·6	8·1	12·6
Pr^i	(M. p. 52—54°)	41·2	8·0	12·9	41·8	8·1	12·6
Bu^n	1·4238	47·6	9·1	11·3	48·1	9·1	10·8
Bu^i	1·4180	47·9	9·1	11·0	48·1	9·1	10·8
Bu^s	1·4151	47·7	9·0	11·1	48·1	9·1	10·8

TABLE 4.

R in $(RO{\cdot}BO)_3$	Time (hr.)	Temp.	Yield (%)	n_D^{22}	n_4^{22}	Found (%) C	Found (%) H	Found (%) B
Me	6	180° (sealed)	98	1·4020	1·233	20·7	5·05	18·9
Et	10	250° (sealed)	98	1·4069	1·113	32·5	6·94	15·3
Pr^n	3	Reflux	93	1·4128	1·017	42·6	8·3	12·3
Pr^i	3	Reflux	93	(M. p. 52—54°)		41·2	7·9	13·0
Bu^n	8	240°	96	1·4236*	1·014*	47·6	8·9	11·2
Bu^i	8	Reflux	95	1·4170	0·997	48·5	9·4	11·2
Bu^s	8	Reflux	96	1·4160	0·985	47·6	9·1	11·0
Ph †	14	400° (sealed)	88	(M. p. 98—101°)		59·2	4·34	9·3

* At 20°. † $C_6H_3O_3B$ requires C, 60·0; H, 4·17; B, 9·0%.

boron trioxide (1·90 g.) were heated under reflux for 6 hr. The supernatant liquid was substantially the orthoborate (Found: B, 4·93. Calc. for $C_{12}H_{27}O_3B$: B, 4·72%). (*b*) Boron trichloride (1·35 g.) in methylene dichloride (10 c.c.) at −80° was added to *tert.*-butyl orthoborate (5·28 g.) in the same solvent (25 c.c.) at −80°. Evaporation of volatile material at 20°/1 mm. left crude boron trioxide (Found: B, 24·3%). (*c*) Addition of water (0·76 g.) in

[17] Thomas, *J.*, 1946, 820.

diethyl ether (10 c.c.) to *n*-butyl orthoborate (9·71 g.) at 20° afforded instantaneously a precipitate of boric acid (Found: B, 18·9%).

Molecular Weights.—These were determined cryoscopically in *cyclo*hexane, in a Beckmann apparatus designed to operate under anhydrous conditions [Found: *M*, 315 (Bu^n), 306 (Bu^i), 305 (Bu^s). $C_{12}H_{27}O_6B_3$ requires *M*, 300].

Infrared Spectra.—The spectra of the metaborates were measured in the region of 2—15 μ on a Grubb–Parsons double-beam spectrometer with a rock-salt prism. With the exception of the two solid compounds (Pr^i, Ph), these were measured in the liquid state. The solids were dissolved in methylene dichloride or carbon disulphide, or dispersed in "Nujol." The spectra of metaborates obtained by the two methods were identical, as follows (max. in $cm.^{-1}$; vs = very strong; s = strong; m = medium; w = weak; sh = shoulder):

Methyl. ~1520 sh, 1486 vs, ~1427 sh, 1351 vs, 1304 s, 1221 w, 1186 w, 1085 s, 1037 m, 1021 sh, 975 w, 898 w, 879 w, 863 w, 799 w, ~736 sh, 718 s.

Ethyl. 1521 sh, 1495 vs, 1433 vs, 1383 vs, 1341 vs, 1289 s, 1215 w, ~1164 w, 1107 s, 1080 s, ~1055 sh, ~961 w, ~824 w, 804 w, ~736 sh, 722 s.

n-*Propyl.* 1520 sh, 1486 vs, 1427 vs, 1355 vs, 1333 vs, 1297 s, 1256 m, 1215 w, 1167 w, 1151 w. 1103 s, 1083 s, 1075 sh, 1052 sh, 1016 w, ~993 w, 969 w, ~911 w, ~889 w, ~870 w, ~734 sh, 722 s.

iso*Propyl.* 1580 sh, ~1508 sh, ~1429 vs, 1406 vs, 1366 vs, 1335 vs, ~1232 sh, 1175 m, 1135 s, 1119 s, 1025 m, ~924 w, 898 m, 789 m, 733 m, 723 s.

n-*Butyl.* 1515 sh, 1488 s, 1425 vs, ~1365 vs, 1344 s, 1299 sh, 1264 sh, 1233 w, 1214 w, 1147 w, 1117 m, 1088 s, 1029 w, 963 w, ~895 w, ~827 w, ~810 w, 734 sh, 723 s.

iso*Butyl.* 1520 sh, 1481 s, 1427 vs, 1385 vs, 1353 vs, ~1337 vs, 1299 s, 1267 s, 1214 w, 1175 w, 1112 m, 1083 s, 1036 m, ~1014 sh, 962 w, ~952 w, 925 w, 908 w, ~876 w, 823 w, ~736 sh, 724 s.

sec.-*Butyl.* 1511 s, ~1459 sh, 1409 vs, 1377 vs, 1337 vs, 1302 s, ~1276 sh, ~1215 w, 1174 m, 1129 s, 1105 s, 1052 m, 1031 sh, ~1005 w, 994 m, ~977 w, 959 w, ~912 w, 865 m, 831 w, 822 m, ~778 w, 735 s, 724 s.

Phenyl. 1592 m, 1494 s, ~1409 sh, 1378 vs, 1355 vs, 1321 s, 1225 s, 1209 m, ~1196 w, 1149 w, ~1096 w, 1068 m, 1020 m, ~1002 w, 977 w, 898 w, ~824 w, 789 w, 757 s, ~715 sh, 700 s, 690 s.

Pyrolysis of n-*Butyl Metaborate.*—The ester (2·34 g.) was heated under reflux at 280—290° for 6 hr. There was no change in appearance, refractive index, or infrared spectrum. In a bromine trap there was collected dibromobutane (0·051 g.), which was separated by washing with sodium thiosulphate, dried, and identified (n_D^{20} 1·5128).

Attempted Distillation of Metaborates.—The results are shown in Table 5. In order to distil the orthoborate at all completely, a bath-temperature about 100° higher than the b. p. of the orthoborate had to be used. The residual boron trioxide was freed from ortho- and metaborates by washing it with diethyl ether.

TABLE 5.

	$(RO)_3B$				B_2O_3 (Calc.: B, 31·1%)	
R in $(RO{\cdot}BO)_3$	Yield (%)	n_D^{20}	Found: B (%)	Calc.: B (%)	Yield (%)	Found: B (%)
Me	91	1·3615	10·2	10·4	100	30·6
Et	92	1·3738	7·3	7·4	98	30·7
Pr^n	92	1·3948	5·8	5·8	100	30·9
Pr^i	93	1·4067	5·8	5·8	99	30·9
Bu^n	92	1·4081	4·7	4·7	100	30·4
Bu^i	94	1·4035	4·8	4·7	100	30·8
Bu^s	92	1·3967	4·7	4·7	99	30·6
Ph	85	(M. p. 92—95°)	3·7	3·7	95	30·2

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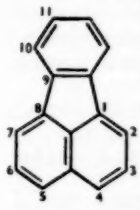
569. *Synthesis of Fluoranthenes. Part XIV.* Synthesis of 3-Methoxyfluoranthene.*

By A. E. Jemmett, S. Horwood Tucker, and (in part) I. Wellings.

3-Methoxyfluoranthene has been synthesised from Cleve's acid, 1-naphthylamine-6-sulphonic acid.

2-, 4-, 10-, and 11-Methoxyfluoranthene have been synthesised [1] but the methods used were not applicable to the synthesis of the remaining isomer, 3-methoxyfluoranthene. This has now been prepared from Cleve's acid, 1-naphthylamine-6-sulphonic acid, by its conversion into 1-acetamido-6-naphthol,[2] thence into 1-iodo-6-methoxynaphthalene.[3] This was converted into 3-methoxyfluoranthene by the standard method of Forrest and Tucker,[4] *viz.*, 1-iodo-6-methoxynaphthalene → 6-methoxy-1-*o*-nitrophenylnaphthalene → amine → 3-methoxyfluoranthene.



Fierz-David and Blangey's method [5] for the separation of Cleve's acids, 1-naphthylamine-6- and -7-sulphonic acid, by means of the sodium salts failed in our hands: instead of the sodium salt of the 7-sulphonic acid being first precipitated, as claimed, we isolated a small amount of a salt whence the benzyl*iso*thiuronium salt of the 6-acid was obtained. A commercial mixture of the mixed sodium salts gave a similar result. Excellent separation was effected by means of the magnesium salts, that of the desired 6-sulphonic acid being almost insoluble in cold water. Improvements have been introduced into the other stages of the synthesis (see below).

An attempt to prepare 3-methoxyfluoranthene from 3-aminofluoranthene [6] was only partially successful. Fluoranthene-3-carboxylic acid has been synthesised, but could not be converted into 3-aminofluoranthene by a Curtius reaction. We failed also to improve on Campbell and Wang's [7] admittedly unsatisfactory synthesis of the above acid, even by use of 9-methylenefluorene.[8] We could not isolate 5-nitro-2-naphthoic acid by the methods of Harrison and Royle; [9] and, since the literature is not clear about the properties of the isomeric nitro-ester,[10] this line was not pursued.

The ultraviolet absorption spectrum of 3-methoxyfluoranthene in ethanol conforms to the theory put forward by Clar, Stubbs, and Tucker [11] regarding the inter-relation of the *p*-band and the position of the methoxyl group on the fluoranthene nucleus.

	p-Bands		*β*-Bands			
$\lambda_{max.}$ (mμ)	364	326	288	280	272	236
log ε	2·88	2·82	3·36	3·31	3·38	3·70

The infrared spectra of the methoxyfluoranthenes have also been examined.[12]

Experimental

Separation of 1-Naphthylamine-6- and -7-sulphonic Acid from a Mixture of Cleve's Acids.—The commercial mixture of Cleve's acids (223 g.) was dissolved in water (2 l.) containing 32%

* Part XIII, *J.*, 1958, 1462.

[1] Hawkins and Tucker, *J.*, 1950, 3286; Stubbs and Tucker, *J.*, 1954, 227.
[2] Campbell, Laforge, and Campbell, *J. Org. Chem.*, 1949, **14**, 351.
[3] Butenandt and Schramm, *Ber.*, 1935, **68**, 2083; Wilds and Close, *J. Amer. Chem. Soc.*, 1947, **69**, 3079.
[4] Forrest and Tucker, *J.*, 1948, 1137.
[5] Fierz-David and Blangey, "Processes of Dye Chemistry," Interscience Publishers Ltd., London, 5th edn., p. 184.
[6] Kloetzel, King, and Menkes, *J. Amer. Chem. Soc.*, 1956, **78**, 1165.
[7] Campbell and Wang, *J.*, 1949, 1513.
[8] Burr, jun., *J. Amer. Chem. Soc.*, 1952, **74**, 1717.
[9] Harrison and Royle, *J.*, 1926, 84.
[10] Graff, *Ber.*, 1883, **16**, 2252; Ekstrand, *J. prakt. Chem.*, 1890, **42**, 273; Elsevier, Vol. **12**, *B*, p. 4167.
[11] Clar, Stubbs, and Tucker, *Nature*, 1950, **166**, 1075; Stubbs and Tucker, ref. 1.
[12] Jemmett, Ph.D. Thesis, Glasgow, 1956.

sodium hydroxide solution (95 ml.). The mixture was stirred with charcoal at 80—90° for 30 min., the insoluble material was removed and washed with boiling water (200 ml.), and the combined filtrates were diluted to 2·2 l. The solution, stirred at 80—90°, was treated with crystalline magnesium sulphate (367 g.) and allowed to cool slowly, the precipitated magnesium 1-naphthylamine-6-sulphonate was filtered off and dissolved in water (2·5 l.) at 80—90°, and 36% hydrochloric acid (140 ml.) slowly added. The precipitated pink powder was washed with water (500 ml.) and dried at 60°, to give 1-naphthylamine-6-sulphonic acid (104 g., 47%).

5-Amino-2-naphthol.—1-Naphthylamine-6-sulphonic acid (40 g.) was added to potassium hydroxide (70 g.) and water (10 ml.) at 250°. The temperature rose rapidly to 270—280°, and was there maintained for ⩾ 7 min. (At 290° decomposition occurs with evolution of ammonia; below 270—280° reaction is incomplete: acid can be recovered.) The fused mass was dissolved in hot water (250 ml.), and the solution acidified, filtered from tar, neutralised with sodium hydroxide solution, and made alkaline with an excess of sodium carbonate, to give 5-amino-2-naphthol as a grey powder, m. p. 186° (25·2 g., 90%). 5-Acetamido-2-naphthol was prepared by suspending the aminonaphthol (16 g.) in boiling benzene (30 ml.) and adding an equivalent amount of acetic anhydride: it crystallised in blades (from methanol), m. p. 215° (100%) (cf. ref. 2).

2-Methoxy-5-o-nitrophenylnaphthalene.—1-Iodo-6-methoxynaphthalene[3] (2·8 g.) and *o*-bromonitrobenzene (2·2 g.) were heated to 180°, and copper powder (3·5 g.) was added with stirring. After 2 hr. at 180° the cooled mass was extracted with benzene, the solvent removed, and the red oil so obtained triturated with ethanol, and crystallised from light petroleum (b. p. 40—60°), then from methanol, as pale green leaflets, m. p. 107—108°, of *2-methoxy-5-o-nitrophenylnaphthalene* (0·8 g., 30%) (Found: C, 72·9; H, 4·9; N, 5·0. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·7; N, 5·0%).

5-o-Aminophenyl-2-methoxynaphthalene.—Reduction of the nitro-compound with hydrogen in presence of Raney nickel in ethanol gave (from ethanol) the *amine*, m. p. 114—115° (*ca.* 100%) (Found: C, 81·7; H, 5·9; N, 5·7. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·1; N, 5·6%).

3-Methoxyfluoranthene.—The amine was dissolved in hot dilute sulphuric acid, and the solution cooled to effect precipitation of small crystals of sulphate which was then diazotised at room temperature. After 30 min. the scarlet solution was heated on the steam-bath with frequent shaking until colourless. The precipitate was filtered off and extracted with hot benzene, and the solution dried and chromatographed on alumina. The yellow eluate (strong blue fluorescence in ultraviolet light) gave *3-methoxyfluoranthene* (50%) as cream crystals (from methanol containing a trace of water), m. p. 83—84° (Found: C, 87·7; H, 5·3. $C_{17}H_{12}O$ requires C, 87·9; H, 5·2%). It gave a *picrate*, orange-yellow needles (from ethanol), m. p. 178° (softening at 175°) (Found: C, 59·7; H, 3·0; N, 9·0. $C_{17}H_{12}O,C_6H_3O_7N_3$ requires C, 59·9; H, 3·3; N, 9·1%), and *complexes* with 1 : 3 : 5-trinitrobenzene, yellow needles (from ethanol–acetic acid), m. p. 178° (softening at 175°) (Found: C, 61·9; H, 3·2. $C_{17}H_{12}O,C_6H_3O_6N_3$ requires C, 62·0; H, 3·4%), and 2 : 4 : 7-trinitrofluorenone (from acetic acid), orange needles, m. p. 219—220° (Found: C, 65·8; H, 3·1. $C_{17}H_{12}O,C_{13}H_5O_7N_3$ requires C, 65·8; H, 3·1%).

Synthesis of Methyl Fluoranthene-3-carboxylate [with I. Wellings].—*5-Iodo-2-naphthoic acid.*[13] Silver sulphate (1 g., theor. 0·78 g.) was dissolved in sulphuric acid (40 ml.) and water (2 ml.) contained in a round-bottomed flask, and cooled to room temperature. 2-Naphthoic acid (0·86 g.) was added, then very finely powdered iodine (1·5 g., theor. 1·3 g.) portionwise whilst the whole was violently stirred by means of a tantalum wire stirrer (a vibro-mixer gave poorer results). After 2 hr., carbon tetrachloride (40 ml.) was added, and stirring continued for 1 hr. The mixture was poured into water (300 ml.), and the precipitated solid filtered through sintered glass. (Since the carbon tetrachloride layer was found to contain only a negligible amount of the desired acid, it was discarded.) The solid was extracted with 5% aqueous potassium hydroxide, and the solution filtered through charcoal, then acidified with dilute sulphuric acid. The precipitate (1·32 g.), after crystallisation from acetone and then from ethyl acetate, gave needles (1·02 g., 66%) of 5-iodo-2-naphthoic acid, m. p. 254° [lit.,[14] m. p. 264° (corr.)]. Preparations on a larger scale gave lower yields (*ca.* 35%). Addition of carbon tetrachloride at the commencement resulted in slightly lower yields: the carbon tetrachloride could not be recovered.

Methyl 5-iodo-2-naphthoate. This was prepared by refluxing pure 5-iodo-2-naphthoic acid

[13] Cf. Derbyshire and Waters, *J.*, 1950, 3694.
[14] Goldstein and Matthey, *Helv. Chim. Acta*, 1937, **20**, 1418.

(4·47 g.) with methanol (60 ml.) containing concentrated sulphuric acid (3 ml.) for 2 hr. The ester crystallised overnight. The filtrate was concentrated to two-thirds its bulk, then poured into ice-cold water. The washed products crystallised from ligroin (b. p. 60—80°) in cream needles (colourless from methanol) (4·2 g., 90%), m. p. 76—78° [lit., 78° (corr.)] (Found: C, 46·0; H, 3·0. Calc. for $C_{12}H_9O_2I$: C, 46·2; H, 2·9%).

When crude 5-iodo-2-naphthoic acid was esterified by hot methanol containing dry hydrogen chloride for 1 hr. and crystallised from much methanol, the first crops (recrystallised from ethanol–methyl cyanide) were of methyl 5 : 8(?)-di-iodo-2-naphthoate, m. p. 164—166° (see below). Later crops, from methanol, gave methyl 5-iodo-2-naphthoate. Chromatography failed to give a satisfactory separation.

5 : 8(?)-*Di-iodo-2-naphthoic acid.* When a greater excess of iodine (and of silver sulphate) was used than that just given, removal of the bulk of the monoiodo-acid by crystallisation from acetone and concentration of the filtrates gave the *di-iodo-acid.* Crystallisation from acetic acid, then from dioxan to which a trace of water was added, gave needles, m. p. 280° (Found: C, 31·3; H, 1·6; I, 59·6. $C_{11}H_6O_2I_2$ requires C, 31·15; H, 1·4; I, 59·9%). Esterification (Fischer–Speier) gave the *methyl ester* (from ethanol–methyl cyanide) as slightly pink needles, m. p. 164—166° (Found: C, 33·0; H, 2·1; I, 58·3. $C_{12}H_8O_2I_2$ requires C, 32·9; H, 1·8; I, 58·0%).

Methyl 5-o-nitrophenyl-2-naphthoate. Methyl 5-iodo-2-naphthoate (1·56 g.), *o*-bromonitrobenzene (1·02 g.), and copper bronze (2 g.) were heated at 180° for 1 hr. whilst stirred by a copper-wire stirrer. Extraction with acetone gave, ultimately, thick, hexagonal, pale yellow plates (from ethyl acetate), m. p. 170—171° (0·51 g., 33%) (Found: C, 70·2; H, 3·8; N, 4·7. $C_{18}H_{13}O_4N$ requires C, 70·35; H, 4·3; N, 4·6%). Results were not improved by use of activated copper.[15]

Methyl 5-o-aminophenyl-2-naphthoate. Raney nickel (1·4 g. of nickel in 7 ml. of ethanol) was saturated with hydrogen; ethyl acetate (previously treated with Raney nickel) was added, then finely powdered methyl 5-*o*-nitrophenyl-2-naphthoate (1·02 g.) was rinsed into the flask by ethyl acetate (20 ml.). Theoretical absorption took place in 30 min. The mixture was boiled and filtered, and the nickel residue thoroughly extracted with boiling ethyl acetate: the amine is nearly insoluble in ethanol. The concentrated filtrates, treated with ethanol, gave stout prisms of *methyl 5-o-aminophenyl-2-naphthoate,* m. p. 146—148° (total, 0·82 g., 90%) (Found: C, 78·2; H, 5·7; N, 5·3. $C_{18}H_{15}O_2N$ requires C, 78·0; H, 5·45; N, 5·05%). When heated in acetic anhydride to the b. p. it gave the *acetyl derivative,* prisms (from a concentrated solution in acetic acid), m. p. 180—181° (Found: C, 75·05; H, 5·2; N, 4·45. $C_{20}H_{17}O_3N$ requires C, 75·2; H, 5·4; N, 4·4%).

Methyl fluoranthene-3-carboxylate. The amino-ester (0·74 g.) was treated in acetic acid (10 ml.) with aqueous sulphuric acid (2 ml. of acid and 8 ml. of water) and then at room temperature with sodium nitrite (0·25 g.) in water (2 ml.). The deep yellow solution was diluted with water (20 ml.), and gave a positive reaction with starch–iodide. Sulphamic acid was added, and the solution warmed on the water-bath. Copper was added. After 10 min. on the boiling-water bath, the solid was collected and extracted with acetone, and the extracts were concentrated to give *methyl fluoranthene-3-carboxylate,* cream needles (from methanol), m. p. 122—123° (Found: C, 82·8; H, 4·4. $C_{18}H_{12}O_2$ requires C, 83·1; H, 4·65%). Further concentration gave a small amount of solid, which on crystallisation from acetic acid and then from ethyl-acetate gave pale greenish-yellow rosettes, m. p. 290° (decomp. from 270°), of fluoranthene-3-carboxylic acid [7] (Found: C, 82·8; H, 4·45. Calc. for $C_{17}H_{10}O_2$: C, 82·9; H, 4·1%). The acetic acid filtrates on slight concentration gave a sandy-coloured product which after crystallisation from benzene, then from acetic acid, gave crystals, m. p. 194—195°, of *methyl 5-o-hydroxyphenyl-2-naphthoate* (Found: C, 77·6; H, 5·0. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%), soluble in 10—50% potassium hydroxide solution only after previous wetting with ethanol. Hydrolysis of methyl fluoranthene-3-carboxylate by boiling 50% potassium hydroxide solution with added ethanol, for 10 min. gave a product which separated reluctantly from ethyl acetate to give pale green crystals (efflorescence) of the above fluoranthene-3-carboxylic acid.

An attempt to prepare 3-aminofluoranthene by a Curtius reaction on fluoranthene-3-carboxylic acid gave in very small amount pale yellow needles, m. p. 115—123°; a mixture with genuine amine [6] (m. p. 128°) softened at 114° but did not melt even at 160°. Unchanged acid was recovered from benzene solutions. An attempt to prepare 3-methoxyfluoranthene from

[15] Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4219.

3-aminofluoranthene [6] gave an unreliable result. In the course of the preparation of the amine by reduction of 4-nitrofluoranthene (first stage) by hydrogen in presence of Raney nickel in ethanol gave a small amount of orange-yellow *NN'-di-4-fluoranthenylhydrazine*, m. p. 303—304° [from benzene (red solution)] (Found: C, 88·8; H, 5·3; N, 6·3. $C_{32}H_{20}N_2$ requires C, 88·9; H, 4·7; N, 6·5%).

4-Acetamido-3-nitrofluoranthene (2·5 g.) was hydrolysed for 30 min. in a boiling mixture of 50% aqueous potassium hydroxide (2 ml.) and 2-methoxyethanol (25 ml.). The deep red solution, diluted with water, gave a brick-red product (2·02 g.) which after crystallisation from ethylene glycol, then from chlorobenzene, and finally from ethyl methyl ketone (during concentration), gave brick-red crystals, softening at 250°, melting at 253° [lit.,[6] 235° (misprint?)] (Found: C, 73·5; H, 4·0; N, 10·8. Calc. for $C_{16}H_{10}O_2N_2$: C, 73·3; H, 3·8; N, 10·7%).

3-Aminofluoranthene was converted in the usual way into the phenol. This was not isolated, but was treated with methyl sulphate in alkali. A very small amount of material was isolated, having m. p. 82° alone or mixed with 3-methoxyfluoranthene. A 2 : 4 : 7-trinitrofluorenone complex had m. p. 205—210°, but a mixture with genuine 3-methoxyfluoranthene complex (m. p. 219—220°) had m. p. 205—210° (quantities obtained were too small to allow further purification).

We thank the Department of Scientific and Industrial Research for a grant (to A. E. J.), and Imperial Chemical Industries Limited for supply of Cleve's acids and the account of the method of separation. Microanalyses were carried out under the supervision of Mr. J. M. L. Cameron by Miss S. U. Watt.

THE UNIVERSITY, GLASGOW. [*Received, February 6th,* 1958.]

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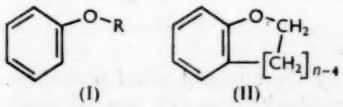
570. *Interdependence of Molecular Conformation and Conjugation in Aromatic Ethers. Part II.*[1]

By G. BADDELEY and J. R. COOKE.

Chroman- and homochroman-2-carboxylic acid have been prepared. The method involved the action of perbenzoic acid on 2-bromo-1-tetralone and 6-bromo-1 : 2-benzosuberone respectively, and the hydrolysis of the resulting bromo-lactones by titration with cold alkali in the presence of hydrogen peroxide.

The ultraviolet absorption spectrum, the rate of bromination, and the acid dissociation constant of homochroman-2-carboxylic acid afford evidence for steric hindrance of conjugation in this compound.

PART I [1] was concerned with conjugation of the oxygen atom and the benzene ring in aromatic ethers mainly of types (I) and (II). The extinction coefficients of the ultraviolet absorption spectra of *tert.*-butoxybenzene and homochroman (II; $n = 7$), the rates of bromination of these ethers, and the rates of solvolysis of their chloromethyl derivatives were shown to be comparatively small. The data were interpreted in terms



(I) (II) (III) (IV)

of the interplanar angle of the ether group and the benzene ring, and the height of the energy barrier to be overcome if coplanarity, the condition for maximum resonance interaction of the ether group and the benzene ring, is to be attained. This paper is concerned

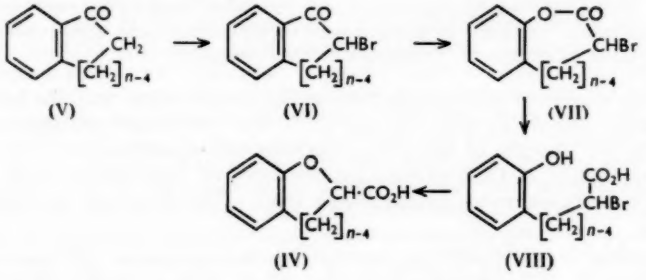
[1] Part I, Baddeley, Smith, and Vickars, *J.*, 1956, 476.

mainly with the corresponding carboxylic acids (IV; $n = 5$, 6, and 7); the acids (III; R = R′ = Me; R = R′ = H; and R = Et, R′ = Me) are included for comparison. The dissociation constants of the acids in water at 25°, the rates of bromination in glacial acetic acid at 20°, and the wavelengths and extinction coefficients of the ultraviolet absorption bands of the acids in hexane are listed in the Table.

Comparison of the ultraviolet absorption spectra, acid dissociation constants, and rates of bromination of the acids.

		Bromination in AcOH		Absorption spectra			
				Max. (Å)		$\varepsilon_{max.}$	
	pK_a	$t_{20\%}$ (min.)	$k_{rel.}$				
Coumaran-2-carboxylic acid	3·25	14·2	30	2850	2790	2375	2670
Chroman-2-carboxylic acid	3·38	26·4	16	2810	2735	1860	1800
Homochroman-2-carboxylic acid	3·63	1920	0·22	2700	2650	555	570
α-*o*-Tolyloxybutyric acid	3·43	33·6	12·5	2775	2710	1170	1300
α-*o*-Tolyloxypropionic acid	3·37	20·8	20	2775	2710	1440	1620
Phenoxyacetic acid	3·35	420	1·0	2760	2700	1140	1275

Comparison of the absorption spectra and rates of bromination of the acids (IV) with those for the ethers (II) (see Part I) shows that the inductive withdrawal of electrons by the carboxyl group from the ether-oxygen atom displaces the absorption bands to shorter wavelengths and lower coefficients of absorption, and decreases the rate of bromination. Increase in the size of the heterocycle from five to seven members affects the ultraviolet absorption spectra of the acids (IV) and ethers (II) similarly, and causes a decrease in the rate of bromination which is somewhat greater in the case of the acids. The results afford evidence for steric hindrance of conjugation in homochroman-2-carboxylic acid similar to that in homochroman. The dissociation constants of the acids provide further evidence of this steric hindrance. Conjugation of the ether-oxygen atom and the benzene ring in the acids involves a displacement of electrons from the oxygen atom to the benzene ring which, by increasing the inductive effect of the oxygen atom, facilitates acid dissociation of the neighbouring carboxyl group. Thus the hindrance of conjugation in homochroman-2-carboxylic acid accounts for the comparatively low acid dissociation constant *i.e.*, high value of pK_a, of this compound.



The acids (IV; $n = 6$ and 7) were afforded by the annexed novel procedure. The bromo-ketones (VI; $n = 6$ and 7), obtained from the ketones (V), reacted slowly with perbenzoic acid in chloroform, to give the bromo-lactones (VII). These were extensively decomposed by hot alkali but were conveniently converted into the bromo-acids (VIII) by addition of hydrogen peroxide and titration with cold sodium hydroxide solution. The cyclised acids (IV; $n = 6$ and 7) were obtained from the bromo-acid (VIII) by the action of hot alkali.

Experimental

Materials.—(i) Coumaran-2-carboxylic acid was prepared [2] from coumarin, and crystallised from light petroleum in needles, m. p. 117—119° (Found: C, 66·1; H, 5·0%; acid equiv., 165. Calc. for $C_9H_8O_3$: C, 66·0; H, 4·9%; equiv., 165).

(ii) *Chroman-2-carboxylic acid* was prepared from 2-bromo-1-tetralone.[3] The latter (15 g.) was allowed to react with perbenzoic acid (19 g.) in chloroform (340 c.c.) at room temperature for 10 days. The mixture was then washed, first, with an aqueous solution of potassium iodide (4 g.) containing 2N-hydrochloric acid (5 c.c.), then with an aqueous solution of sodium thiosulphate (2·5 g.) and, finally, several times with sodium hydrogen carbonate solution. The chloroform layer was separated and dried ($MgSO_4$), and the chloroform was removed by distillation. The residue, a pale yellow oil (11·7 g.), was dissolved in ethanol (40 c.c.) containing one drop of phenolphthalein solution, 90% hydrogen peroxide solution (5 c.c.) was carefully added, and the mixture was neutralised with 2N-sodium hydroxide (~20 c.c.). The mixture was poured into water (250 c.c.), the whole washed with ether, and the aqueous layer acidified and extracted with ether. The extract was dried ($MgSO_4$) and evaporated. The residue, a pale yellow oil (5 g.), was heated on a steam-bath for 45 min. with 2N-sodium hydroxide (20 c.c.). The mixture was cooled, washed with ether, acidified, and extracted with ether. This extract was dried ($MgSO_4$) and gave a pale brown solid (2·9 g.) by evaporation. The product was dissolved in the minimum amount of sodium hydrogen carbonate solution, and the equivalent amount of dilute hydrochloric acid was added in four parts with ether-extraction after each addition. The first three extracts gave the required acid (1·3 g.), m. p. 90—95°; the fourth gave resin. The acid was purified chromatographically in the manner described by Bhargava and Heidelberger [4] and crystallised from light petroleum in colourless needles, m. p. 98·5—100° (Found: C, 67·6; H, 5·2%; acid equiv., 176. $C_{10}H_{10}O_3$ requires C, 67·4; H, 5·6%; equiv., 178).

(iii) *Homochroman-2-carboxylic acid* was similarly prepared from *4-bromo-1 : 2-benzocyclohepten-3-one*. This bromo-ketone (24 g.) was obtained in 90% yield from benzosuberone [5] by the procedure described [3] for the preparation of 2-bromo-1-tetralone; it is a colourless oil, b. p. 115·5—116°/0·3 mm. (Found: C, 55·2; H, 4·8; Br, 33·4. $C_{11}H_{11}OBr$ requires C, 55·2; H, 4·6; Br, 33·5%). The required acid (1·85 g.) separated from light petroleum in needles, m. p. 100—102·5° (Found: C, 68·9; H, 5·8%; acid equiv., 195. $C_{11}H_{12}O_3$ requires C, 68·8; H, 6·25%; equiv., 192).

(iv) Phenoxyacetic and α-*o*-tolyloxy-propionic and -butyric acid were prepared and purified as previously described.

Ultraviolet Absorption Spectra.—Solutions (0·0005M) of the acids in hexane [6] and a Hilger "Uvispek" photoelectric spectrophotometer were used.

Rates of Bromination.—The time intervals for 20% bromination of the acids in glacial acetic acid at 20°, the initial solutions being 0·001M with respect to bromine and 0·01M with respect to aromatic acid, were determined by the procedure described by de la Mare and Vernon.[7]

pK_a *Values for the Acids.*—These were determined for 0·005M-solutions in water at 25° by potentiometric titration, a Cambridge Portable Laboratory pH Meter of accuracy 0·01 pH unit being used.

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[2] *Org. Synth.*, 1944, **24**, 33; Fittig and Ebert, *Annalen*, 1883, **216**, 166; Stoermer and Konig, *Ber.*, 1906, **39**, 493.
[3] Wilds and Johnson, *J. Amer. Chem. Soc.*, 1946, **68**, 87.
[4] Bhargava and Heidelberger, *ibid.*, 1955, **77**, 166.
[5] Aspinall and Baker, *J.*, 1950, 745.
[6] Graff, O'Connor, and Skau, *Ind. Eng. Chem. Analyt.*, 1944, **16**, 556.
[7] de la Mare and Vernon, *J.*, 1951, 1764.

XUM

571. *Cytotoxic Compounds. Part I.* p-(NN-*Di*-2′-*chloroethyl- and* p-(NN-*Di*-2′-*bromoethyl-amino*)*thiophenol.*

By M. H. Benn, L. N. Owen, and (in part) A. M. Creighton.

p-(*NN*-Di-2-chloroethylamino)thiophenol has been synthesised by several methods; the preferred route involves thiocyanation of *NN*-di-2′-chloroethylaniline, followed by reduction. The bromo-analogue is obtained in a similar way. Derivatives, including mixed disulphides, have been prepared, in some of which the cytotoxic unit is linked to a sugar or steroid.

In contrast to the effect of a *p*-hydroxy-group, which is known to increase the reactivity of the chloroethyl groups in *p*-(*NN*-di-2-chloroethylamino)phenol (in comparison with *NN*-di-2′-chloroethylaniline), the *p*-thiol group causes slight deactivation.

Many of the so-called " nitrogen mustards," $R{\cdot}N(CH_2{\cdot}CH_2Cl)_2$, which have been synthesised in large numbers during the last ten years,[1] show cytotoxic effects on proliferating cells and can inhibit the growth of tumours, but unfortunately their toxicity towards normal tissue renders them unsuitable for prolonged chemotherapeutic use.[2] Danielli [3,4] has pointed out that more favourable selectivity of action on a tumour might be achieved by designing the structure of a " nitrogen mustard " so as to take advantage of certain differences which may exist between neoplastic and healthy cells. The principle of enzymic activation falls into this category, and has already been exploited. Thus [4,5] *NN*-di-2′-chloroethyl-*p*-phenylenediamine (I) is active against the Walker rat carcinoma but has a high general toxicity; the introduction of electron-withdrawing acyl groups, as in the *N*′-acetyl (II) and the *N*′-benzoyl derivative, results in a pronounced reduction both in the reactivity of the halogen atoms and in the toxicity, but only the acetyl derivative retains any significant effect on the tumour. Since the tumour is known to possess an enzyme which can deacylate an acetamido- but not a benzamido-group [4] it is likely that the activity of the acetyl derivative is due to the liberation of the parent " nitrogen mustard " (I) by enzymic fission at the site of the tumour. Several other types of derivative, based on this principle, have been described.[5,6]

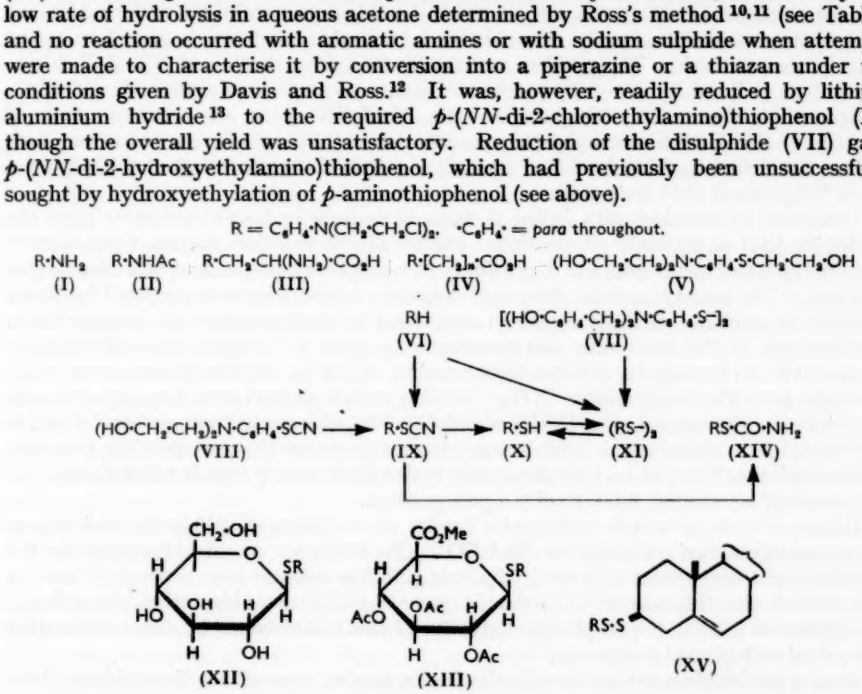
A second possible exploitation of differences in cellular properties lies in the principle of active transport,[3,4] *i.e.*, utilisation of the selectivity which a cell may show for a particular type of molecule, an approach which involves the preparation of compounds in which a " nitrogen mustard " is linked to a physiologically important substance; interesting examples are the phenylalanine derivative (III),[7] the acids (IV),[8] and *NN*-di-2′-chloroethyl-D-glucosamine.[9]

The present series of papers will record syntheses of compounds some of which possess structures based on the principles outlined above. The results of biological tests, carried out under the direction of Professor J. F. Danielli, F.R.S., will be described elsewhere.

Many of the aromatic " nitrogen mustards " hitherto reported have been derivatives of the *p*-amino-compound (I) or of the corresponding phenol. In view of the importance of thiol groups in biological systems, the thiol analogue (X) would be of much interest, and several possible routes to this compound were investigated. *p*-Aminophenol reacts with ethylene oxide in aqueous acetic acid to give *p*-(*NN*-di-2-hydroxyethylamino)phenol,[5] but

[1] See, *inter al.*, Ross, *J.*, 1949, 183, and many subsequent papers; Wilson and Tishler, *J. Amer. Chem. Soc.*, 1951, **73**, 3635.
[2] Klopp and Bateman, *Adv. Cancer Res.*, 1954, **2**, 255; Stock, *ibid.*, p. 425.
[3] Danielli, *Nature*, 1952, **170**, 863.
[4] *Idem*, Ciba Foundation Symposium, " Leukaemia Research," Churchill, London, 1954, p. 263.
[5] Ross, Warwick, and Roberts, *J.*, 1955, 3110.
[6] Ross and Warwick, *J.*, 1956, 1364.
[7] Bergel and Stock, *J.*, 1954, 2409; Bergel, Burnop, and Stock, *J.*, 1955, 1223.
[8] Everett, Roberts, and Ross, *J.*, 1953, 2386.
[9] Vargha, Fehér, and Lendval, *J.*, 1957, 810.

under these conditions *p*-aminothiophenol underwent hydroxyethylation at the thiol group also and gave *NNS*-tri-2-hydroxyethyl-*p*-aminothiophenol (V). Attention was therefore directed to syntheses in which the thiol group could be introduced at a later stage. Hydroxyethylation of di-*p*-aminophenyl disulphide gave the tetrol (VII), but replacement of the hydroxyl groups by chlorine was difficult because of its low solubility in the usual solvents; the method finally adopted was to heat it with phosphorus oxychloride without a solvent, which gave, in poor yield, di-[*p*-(*NN*-di-2-chloroethylamino)phenyl] disulphide (XI). The halogen atoms in this compound were relatively unreactive, as shown by the low rate of hydrolysis in aqueous acetone determined by Ross's method [10,11] (see Table), and no reaction occurred with aromatic amines or with sodium sulphide when attempts were made to characterise it by conversion into a piperazine or a thiazan under the conditions given by Davis and Ross.[12] It was, however, readily reduced by lithium aluminium hydride [13] to the required *p*-(*NN*-di-2-chloroethylamino)thiophenol (X), though the overall yield was unsatisfactory. Reduction of the disulphide (VII) gave *p*-(*NN*-di-2-hydroxyethylamino)thiophenol, which had previously been unsuccessfully sought by hydroxyethylation of *p*-aminothiophenol (see above).



Holzmann [14] prepared di-[*p*-(*NN*-diethylamino)phenyl] disulphide by direct sulphuration of *NN*-diethylaniline with sulphur monochloride, and an attempt was therefore made to prepare the disulphide (XI) by a similar reaction on *NN*-di-2′-chloroethylaniline (VI) in the presence of pyridine (to avoid loss of the amine as hydrochloride). This gave a non-crystalline product in which the presence of the disulphide (XI) was established by reduction with lithium aluminium hydride and characterisation of the resulting thiol (X). The non-crystallinity of the disulphide and of the thiol obtained by this route was probably due to the presence of the *ortho*-isomer; it is significant that the disulphide obtained by Holzmann [14] from *NN*-diethylaniline was less pure than that which can be obtained by oxidation of *p*-*NN*-diethylaminothiophenol (see below).

The production of the thiol group by reduction of a thiocyanate was next investigated. Hydroxyethylation of *p*-thiocyanatoaniline with ethylene oxide in aqueous acetic acid was slow owing to the diminished basic character of the amino-group, and after the normal time

[10] Ross, *J.*, 1949, 183.
[11] Everett and Ross, *J.*, 1949, 1972.
[12] Davis and Ross, *J.*, 1949, 2381; Ross, *J.*, 1950, 815.
[13] Cf. Arnold, Lien, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 731.
[14] Holzmann, *Ber.*, 1887, **20**, 1636.

required for bishydroxyethylation only the *N*-2-hydroxyethyl compound was isolated, but by prolonged reaction *NN*-di-2′-hydroxyethyl-*p*-thiocyanatoaniline (VIII) was obtained. A more convenient method, however, was thiocyanation [15] of the readily available *NN*-di-2′-hydroxyethylaniline. Reaction of the diol (VIII) with phosphorus oxychloride in benzene gave a non-crystalline product which contained the desired thiocyanato-compound (IX) since on reduction with lithium aluminium hydride [16] it gave a product from which crystalline derivatives of the thiol (X) could be readily obtained.

It seemed likely that the difficulty in obtaining pure products, with both the disulphide and the thiocyanate route, was due to the rather vigorous conditions under which the halogen atoms were introduced; it would thus be desirable to effect this step at an earlier stage in the synthesis. The problem was finally solved by the use of *NN*-di-2′-chloroethylaniline (VI), which is readily prepared [17] in a pure state from aniline *via* *NN*-di-2′-hydroxyethylaniline. On thiocyanation this dichloride gave an excellent yield of crystalline *NN*-di-2′-chloroethyl-*p*-thiocyanatoaniline (IX), which on reduction with lithium aluminium hydride furnished crystalline *p*-(*NN*-di-2-chloroethylamino)thiophenol (X) in 75% overall yield from aniline.

Oxidation of the thiol with iodine in aqueous sodium hydrogen carbonate gave the disulphide (XI) as an easily crystallisable solid. This is therefore the most satisfactory route to the latter compound, the crystallinity of which is very dependent on a high degree of purity. The *S*-acetyl and the *S*-benzoyl derivative of the thiol were prepared by direct acylation in pyridine, and the *S*-methyl compound by methylation with diazomethane. Condensation of the thiol with acetobromoglucose gave *p*-(*NN*-di-2-chloroethylamino)-phenyl 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-thioglucoside, which by base-catalysed solvolysis in methanol gave the thioglucoside (XII). Similarly, with methyl acetobromoglucuronate the thiol gave the methyl ester (XIII) of *S*-*p*-(*NN*-di-2-chloroethylamino)phenyl 2 : 3 : 4-tri-*O*-acetyl-β-D-thioglucuronic acid, but an attempt to obtain the corresponding free acid, by deacetylation followed by hydrolysis with hydrochloric acid (towards which thioglucosides are relatively stable), failed to give a pure product.

Biological tests on certain carbamates having proved interesting,[18] it was desirable to obtain analogues derived from the thiol (X). The formation of thiocarbamates by the hydrolysis of thiocyanates with 95% sulphuric acid has recently been reported,[19] and by this method the thiocyanate (IX) readily gave *S*-*p*-(*NN*-di-2-chloroethylamino)phenyl thiocarbamate (XIV); the *N*′-phenyl derivative of this was obtained by direct interaction of the thiol with phenyl *iso*cyanate.

Since a disulphide is subject to reductive fission *in vivo*, some mixed disulphides derived from the " thiol-mustard " (X) with other thiols were synthesised. Such compounds are commonly prepared [20] by interaction of a thiol with a sulphenyl halide or sulphenyl thiocyanate, though the yields are very variable because often the two symmetrical disulphides are also formed. The sulphenyl halides are normally obtained by direct interaction of halogen and a thiol or disulphide, but although treatment of the disulphide (XI) in carbon tetrachloride with chlorine gave an orange-red solution, indicating the formation of a sulphenyl chloride, the product rapidly decomposed; similar treatment of the thiol (X) was also unsuccessful, possibly because the liberated hydrogen chloride precipitated the base as hydrochloride. Recently the use of *N*-bromo- or *N*-chloro-succinimide in the preparation of sulphenyl halides has been described; [21] this method is useful when the

[15] Cf. Wood, *Organic Reactions*, 1946, **3**, 240.
[16] Cf. Strating and Backer, *Rec. Trav. chim.*, 1950, **69**, 638, 909.
[17] Robinson and Watt, *J.*, 1934, 1536.
[18] Danielli, Hamilton, May, and Barnard, *Ann. Rep. British Empire Cancer Campaign*, 1956, **34**, 398.
[19] Riemschneider, Wojahn, and Orlick, *J. Amer. Chem. Soc.*, 1951, **73**, 5905.
[20] Lecher, *Ber.*, 1920, **53**, 577; Lecher and Simon, *Ber.*, 1921, **54**, 632; Lecher and Wittwer, *Ber.*, 1922, **55**, 1474; Kharasch, Potempa, and Wehrmeister, *Chem. Rev.*, 1946, **39**, 269; Schöberl and Wagner in Houben-Weyl, " Methoden der Organischen Chemie," 4th edn., Georg Thieme Verlag, Stuttgart, 1955, vol. IX, p. 263.
[21] Emde, D.R.-P. 804,572; *Chem. Abs.*, 1952, **46**, 529.

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formation of hydrogen halide has to be avoided. Treated in this way the thiol (X) gave red solutions which probably contained the sulphenyl halide, but after further reaction with other thiols (thiophenol, ethanedithiol, or thiocholesterol) only the two symmetrical disulphides could be isolated.

It is recognised [22] that sulphenyl halides may be unstable in the presence of tertiary amines, and this probably accounts for the lack of success in the above experiments; the alternative approach, involving the formation of a sulphenyl halide from the other component, was therefore investigated. Reaction of thiocholesterol (3-β-mercaptocholest-5-ene) * with *N*-chlorosuccinimide in benzene, followed by addition of the " thiol-mustard " (X), gave a mixture which was separated by chromatography on alumina into di(cholest-5-en-3β-yl) disulphide, di-[*p*-(*NN*-di-2-chloroethylamino)phenyl] disulphide (XI), and *p*-(*NN*-di-2-chloroethylamino)phenyl cholest-5-en-3β-yl disulphide (XV), the yield of the mixed disulphide being 30%. Similar treatment of 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-thioglucose with *N*-bromosuccinimide, followed by reaction with the " thiol-mustard," gave a 43% yield of 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucosyl *p*-(*NN*-di-2-chloroethylamino)phenyl disulphide. 2 : 4-Dinitrobenzenesulphenyl chloride reacted smoothly with the " thiol-mustard " to give *p*-(*NN*-di-2-chloroethylamino)phenyl 2 : 4-dinitrophenyl disulphide.

The result of biological tests [18] on the thiol (X) and its derivatives, some of which showed very low toxicities, indicated that a study should be made on compounds of greater reactivity, and some 2-bromoethyl analogues were therefore synthesised. Crystalline *p*-(*NN*-di-2-bromoethylamino)thiophenol [bromo-analogue of (X)] was prepared from *NN*-di-2′-bromoethylaniline, *via* the thiocyanate, by the same methods as those used to effect the conversions (VI) ⟶ (IX) ⟶ (X). Controlled hydrolysis of the thiocyanate gave the thiocarbamate [bromo-analogue of (XIV)]. Oxidation of the bromo-thiol with iodine gave the corresponding disulphide, whilst reaction with diazomethane and with 2 : 4-dinitrobenzenesulphenyl chloride furnished the *S*-methyl ether and *p*-(*NN*-di-2-bromoethylamino)phenyl 2 : 4-dinitrophenyl disulphide, respectively. These bromoethyl compounds are markedly more vesicant than the chloroethyl analogues, and consequently require more careful manipulation.

The extent of hydrolysis of the mustards after 30 min. in boiling 1 : 1 aqueous acetone was determined by Ross's method [10,11] (see Table); when possible, a concentration of *ca.* 0·01M was used, though for sparingly soluble compounds it was necessary to use more dilute solutions and in such cases the results are probably slightly high (cf. refs. 10 and 11). When determinations of both hydrogen ion and halide ion were made the agreement was good, indicating [10] the absence of quaternary halide formation during the hydrolysis of these aromatic " nitrogen-mustards." The parent unsubstituted *NN*-di-2′-chloroethylaniline undergoes 20% hydrolysis under these conditions [10] and it is interesting that the introduction of the *p*-thiol group has a slight deactivating effect; this is in marked contrast to the figure reported [5] for the *p*-hydroxy-analogue (56%), and demonstrates the lack of electron-donation by sulphur towards the aromatic ring. Acylation of the thiol produces the expected reduction in reactivity, and the electron-withdrawing power of the thiocyanato-group is also evident. The figures also show the considerably increased reactivity of the *NN*-di-2′-bromoethyl compounds compared with that of the chloro-analogues, though the deactivating effect of the substituents is again similar since the figure for the parent *NN*-di-2′-bromoethylaniline [10] is 79%.

It was important in the biological tests to establish whether the enzyme systems present in the neoplastic tissue were capable of releasing the " thiol-mustard " (X) from its derivatives. This information is conveniently obtained by the use of model

* We provisionally accept the 3β-configuration proposed by O'Connor and Nace (*J. Amer. Chem. Soc.*, 1953, **75**, 2118), though this may require modification (cf. Pierce, Richards, Shoppee, Stephenson, and Summers, *J.*, 1955, 694).

[22] Moore and Johnson, *J. Amer. Chem. Soc.*, 1935, **57**, 1517; Kharasch, McQuarrie, and Buess, *ibid.*, 1953, **75**, 2658.

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(" non-mustard ") compounds, and for this purpose *p*-(*NN*-diethylamino)thiophenol was synthesised by reduction of *NN*-diethyl-*p*-thiocyanatoaniline; it was converted into its disulphide, its *S*-acetyl derivative, and *p*-(*NN*-diethylamino)phenyl 2 : 4-dinitrophenyl disulphide. The thioglucoside has already been described.[23]

R = *p*-(*NN*-Di-2-chloroethylamino)phenyl. R′ = *p*-(*NN*-Di-2-bromoethylamino)phenyl.

Compound	mmole in 25 c.c. of acetone + 25 c.c. of water	Hydrolysis in 30 min. at 66° H^+ (%)	Hal^- (%)	Footnote
R·SH	0·2	15	—	*a*
$(R·S·)_2$	0·04	6	8	*b*, *c*
R·SAc	0·4	3	—	*a*
R·SBz	0·1	2	—	*a*
R·SMe	0·5	13	13	*b*, *c*
R·SCN	0·4	3	3	*b*, *c*
R·S·CO·NH_2	0·2	*ca.* 8	—	*a*
R·S· (tetra-acetylglucosyl)	0·5	6	6	*b*, *c*
R·S· (glucosyl)	0·4	7	7	*b*, *c*
R·S·S· (tetra-acetylglucosyl)	0·3	6	5	*b*, *c*
R·S·S· (cholesteryl)	0·2 [e]	5	—	*b*
R′·SH	0·1	70	—	*a*
$(R′·S·)_2$	0·03	56	56	*b*, *d*
R′·SCN	0·5	19	19	*b*, *d*
R′·S·CO·NH_2	0·2	40	—	*a*

[a] H^+ titrated potentiometrically (glass electrode). [b] H^+ titrated to phenolphthalein indicator. Cl^- titrated to chromate indicator. [d] Br^- titrated to eosin indicator. [e] In 125 c.c. of acetone +25 c.c. of water at 62°.

Experimental

Microanalyses were by Miss J. Cuckney and the staff of the Organic Chemistry Microanalytical Laboratories.

NN-Di-2′-hydroxyethylaniline.—Aniline (250 g.), 4N-aqueous acetic acid (150 c.c.) (cf. ref. 8) and ethylene oxide (250 c.c.) were mixed together, with cooling, and stirred overnight. More ethylene oxide (250 c.c.) was then added and stirring continued for a further 24 hr. The mixture was neutralised with aqueous sodium carbonate and extracted with chloroform (3 × 250 c.c.) to give an oil, which was fractionally distilled under nitrogen. *NN*-Di-2′-hydroxyethylaniline was obtained as the fraction, b. p. 170—175°/0·3 mm., 165—168°/0·2 mm., m. p. 57—58° (441 g., 91%) (lit.,[10, 24] b. p. 175—180°/3 mm., m. p. 58°). Yields were invariably excellent, 90—96%. It was converted into *NN*-di-2′-chloroethylaniline, m. p. 45—47°, by Robinson and Watt's [17] method.

p-*Aminophenyl* 2 : 4-*Dinitrophenyl Sulphide.*—Prepared by reaction of *p*-aminothiophenol [25] with chloro-2 : 4-dinitrobenzene in alkaline aqueous ethanol, this crystallised from ethanol in orange-red needles, m. p. 167—168° (Found: C, 49·6; H, 3·3; N, 14·4. $C_{12}H_9O_4N_3S$ requires C, 49·5; H, 3·1; N, 14·4%).

Di-(p-*aminophenyl*) *Disulphide.*—Aerial oxidation of an aqueous alkaline solution of *p*-aminothiophenol, in the dark, gave an almost theoretical yield of the disulphide, which crystallised from aqueous ethanol in yellow needles, m. p. 76—77° (lit.,[26] m. p. 76—77°).

When di-(*p*-aminophenyl) disulphide was tetrazotised in ice-cold 2N-hydrochloric acid, and coupled with β-naphthol in sodium hydroxide solution, *di-*[p-(2-*hydroxy*-1-*naphthylazo*)*phenyl*] *disulphide* was precipitated; recrystallisation from ethyl acetate gave red needles, m. p. 251° (Found: N, 10·1. $C_{32}H_{22}O_2N_4S_2$ requires N, 10·0%).

NNS-*Tri-*(2-*hydroxyethyl*)-p-*aminothiophenol.*—A suspension of *p*-aminothiophenol (10 g.) in 2N-aqueous acetic acid (50 c.c.) was cooled to 0°, ethylene oxide (30 c.c.) was added, and the mixture was stirred overnight. The homogeneous solution was then neutralised with saturated aqueous sodium hydrogen carbonate, and the precipitated oil was separated, taken up in ethanol, and dried (Na_2SO_4); evaporation of the solvent gave a yellow oil, which showed no reaction for a free thiol. A portion was distilled at 240° (bath)/0·02 mm.; the distillate slowly solidified, and on recrystallisation from *iso*propyl alcohol gave NNS-*tri-*(2-*hydroxyethyl*)-p-*aminothiophenol*,

[23] Montgomery, Richtmyer, and Hudson, *J. Org. Chem.*, 1946, **11**, 301.
[24] Gabel, *Ber.*, 1925, **58**, 577.
[25] Gilman and Gainer, *J. Amer. Chem. Soc.*, 1949, **71**, 1749.
[26] Hinsberg, *Ber.*, 1905, **38**, 1133; cf. Schmidt, *Ber.*, 1878, **11**, 1172.

white prisms, m. p. 59° (Found: C, 56·0; H, 7·4; N, 5·1; O, 18·2. $C_{12}H_{19}O_3NS$ requires C, 56·0; H, 7·4; N, 5·4; O, 18·65%).

Di-[p-(NN-*di*-2-*hydroxyethylamino*)*phenyl*] *Disulphide*.—A solution of di-(*p*-aminophenyl) disulphide (30 g.) in ethylene oxide (100 c.c.) and 4N-aqueous acetic acid (20 c.c.) was stirred overnight; the crude product usually separated as an oil or semi-solid mass. Excess of ethylene oxide was removed under reduced pressure, and the residue was neutralised with saturated aqueous sodium hydrogen carbonate, saturated with salt, and extracted with ethyl acetate (4 × 150 c.c.). The extracts were dried (Na_2SO_4) and evaporated to a syrup, which was tested for the presence of primary aromatic amine by diazotisation and coupling with β-naphthol; if positive, the syrup was re-treated with ethylene oxide (65 c.c.) and 4N-aqueous acetic acid (12 c.c.) overnight and worked up as described above. A solution of the product in hot aqueous ethanol (charcoal) deposited feathery yellow crystals (60—75%) of *di*-[p-(NN-*di*-2-*hydroxyethylamino*)*phenyl*] *disulphide*, m. p. 136—138°. Recrystallised from aqueous ethanol it had m. p. 138—140° (Found: C, 56·4; H, 6·9; N, 6·6; S, 15·45; O, 15·35. $C_{20}H_{28}O_4N_2S_2$ requires C, 56·6; H, 6·65; N, 6·6; S, 15·1; O, 15·1%).

The *dipicrate*, which crystallised from methanol–ether as a yellow powder, m. p. 91—93°, readily lost picric acid when heated *in vacuo* (Found, on a sample dried *in vacuo* at 20°: C, 43·6; H, 4·6; N, 12·1. $C_{32}H_{34}O_{18}N_8S_2$ requires C, 43·5; H, 3·9; N, 12·7%). The *tetrabenzoate* (prepared by benzoyl chloride–pyridine) after recrystallisation from pyridine formed an amorphous white powder, m. p. 269—270° (Found: C, 68·25; H, 5·2. $C_{48}H_{44}O_8N_2S_2$ requires C, 68·55; H, 5·3%).

Di-[p-(NN-*di*-2-*chloroethylamino*)*phenyl*] *Disulphide*.—(i) *From di*-[p-(NN-*di*-2-*hydroxyethylamino*)*phenyl*] *disulphide*. The tetrol (10 g.) and phosphorus oxychloride (20 c.c.) were mixed together. There was an immediate exothermic reaction with evolution of hydrogen chloride. After this had ceased the mixture was heated under reflux on a steam-bath for 30 min., and the excess of phosphorus oxychloride was then distilled off under reduced pressure. The residual green syrup was triturated with benzene and saturated aqueous sodium hydrogen carbonate until it had entirely dissolved; the benzene solution was dried (Na_2SO_4) and concentrated under reduced pressure to an oil which was chromatographed on acid-washed alumina, with benzene as eluant. The well-defined yellow band was eluted, and concentration of the eluates gave a yellow oil which deposited crystals (3·4 g., 31%), m. p. 70·5—71·5°, when set aside overnight in benzene–light petroleum (b. p. 40—60°) (1 : 2). Recrystallisation from the same solvent gave *di*-[p-(NN-*di*-2-*chloroethylamino*)*phenyl*] *disulphide*, m. p. 71—72°, raised to 76° on recrystallisation from ether–light petroleum (b. p. 40—60°), as yellow prisms (Found: C, 48·0; H, 5·1; N, 5·5; S, 13·35; Cl, 28·1. $C_{20}H_{24}N_2S_2Cl_4$ requires C, 48·2; H, 4·85; N, 5·6; S, 12·9; Cl, 28·5%). Yields were 19—50% and there was often considerable difficulty in initiating crystallisation.

(ii) *From* NN-*di*-2′-*chloroethylaniline*. To a solution of *NN*-di-2′-chloroethylaniline (40 g.) and pyridine (14·7 g.) in chloroform (100 c.c.), redistilled sulphur monochloride (12·5 g.) in chloroform (100 c.c.) was added dropwise (30 min.), with stirring, at 10°. Stirring was continued for a further 1½ hr., and the mixture was then washed with water, dried (Na_2SO_4), and concentrated to a syrup. Chromatography in benzene on alumina gave crude di-[*p*-(*NN*-di-2-chloroethylamino)phenyl] disulphide as a yellow syrup (49 g.), characterised by reduction to the thiol (see below) and conversion into *p*-(*NN*-di-2-chloroethylamino)phenyl 2 : 4-dinitrophenyl sulphide, m. p. and mixed m. p. 156°.

(iii) *From* p-(NN-*di*-2-*chloroethylamino*)*thiophenol*. The thiol (2·0 g.) (see below) was dissolved in benzene (50 c.c.), and shaken with saturated aqueous sodium hydrogen carbonate (50 c.c.) during the addition of a solution of iodine in aqueous potassium iodide until the iodine colour persisted. The benzene layer was washed with aqueous sodium thiosulphate, dried (Na_2SO_4), and evaporated to a syrup. Chromatography gave the disulphide as yellow needles (1·67 g., 83%), m. p. 78—79° (from ethanol).

Treatment of the disulphide with picric acid in methanol, ethanol, or ether failed to give a crystalline picrate. It was also recovered largely unchanged (m. p. and mixed m. p. *ca.* 72°) after being refluxed for 4 hr. with aniline in aqueous acetone. No product was obtained with *p*-toluidine or with sodium sulphide under the same conditions, though in these cases the unchanged chloroethylamine was not obtained crystalline.

N-2′-*Hydroxyethyl*-p-*thiocyanatoaniline*.—A suspension of *p*-thiocyanatoaniline [27] (17 g.),

[27] Kaufmann and Oehring, *Ber.*, 1926, **59**, 187.

ethylene oxide (25 c.c.), and 2N-aqueous acetic acid (25 c.c.) was stirred at room temperature. After 4 hr. more ethylene oxide (10 c.c.) was added, and the clear solution so obtained was stirred for a further 4 hr.; the excess of ethylene oxide was then removed under reduced pressure. The oil which separated solidified (m. p. 40—70°) but it gave a positive test for primary aromatic amine. It was therefore re-treated with ethylene oxide (40 c.c.) and 2N-aqueous acetic acid (15 c.c.) overnight, and the product, isolated as before, was dissolved in ether, washed with saturated aqueous sodium hydrogen carbonate, and dried (Na_2SO_4). Removal of the solvent gave a solid (16 g., 73%), m. p. 95—100°, which on recrystallisation from aqueous methanol (charcoal) gave N-2′-*hydroxyethyl*-p-*thiocyanatoaniline* as white leaflets, m. p. 104° (Found: C, 55·6; H, 5·2; N, 14·8. $C_9H_{10}ON_2S$ requires C, 55·6; H, 5·2; N, 14·4%).

NN-*Di*-2′-*hydroxyethyl*-p-*thiocyanatoaniline*.—(i) *From* p-*thiocyanatoaniline*. *p*-Thiocyanatoaniline (10 g.) was dissolved in ethylene oxide (50 c.c.), 2N-aqueous acetic acid (20 c.c.) was added, and the solution was stirred for 40 hr., more ethylene oxide (20 c.c.) being added after 20 hr. to replace that lost by evaporation. The excess of ethylene oxide was removed under reduced pressure and the residue neutralised with solid sodium hydrogen carbonate. The oil which separated was dissolved in ethyl acetate and dried (Na_2SO_4), and the solvent removed to yield a solid (12 g., 76%). NN-*Di*-2′-*hydroxyethyl*-p-*thiocyanatoaniline* crystallised from ether in needles, m. p. 63° (Found: C, 55·35; H, 5·95; N, 11·6; S, 13·2. $C_{11}H_{14}O_2N_2S$ requires C, 55·4; H, 5·9; N, 11·8; S, 13·5%).

(ii) *From* NN-*di*-2′-*hydroxyethylaniline*. A solution of *NN*-di-2′-hydroxyethylaniline (18·0 g.) and potassium thiocyanate (30 g.) in acetic acid (200 c.c.) was stirred at *ca.* 12° whilst a solution of bromine (16·0 g.) in acetic acid (50 c.c.) was slowly added (20 min.) below the surface of the solution. Stirring was continued for a further 10 min. and the mixture was filtered to remove polymeric material, the filter-cake being washed with ether–ethanol (2 : 1) (100 c.c.); the combined filtrate and washings were neutralised with saturated aqueous sodium carbonate and extracted with ethyl acetate to give a yellow oil (20 g., 86%), which crystallised on trituration with ether. Recrystallisation from aqueous methanol (charcoal) gave needles of *NN*-di-2′-hydroxyethyl-*p*-thiocyanatoaniline, m. p. 61—63° undepressed with the material prepared as above.

The compound is very soluble in ethanol, methanol, propan-2-ol, and ethyl acetate, sparingly soluble in benzene and ether. It gave a *picrate*, lemon-yellow prisms, m. p. 99—100° (from methanol–ether) (Found: C, 43·75; H, 3·8; N, 14·6. $C_{17}H_{17}O_9N_5S$ requires C, 43·7; H, 3·7; N, 15·0%).

p-(NN-*Di*-2-*hydroxyethylamino*)*thiophenol*.—Di-[*p*-(*NN*-di-2-hydroxyethylamino)phenyl] disulphide (8·0 g.) in concentrated hydrochloric acid (50 c.c.) was heated on a steam-bath and stirred whilst zinc dust was added in portions (5 × 4 g.) during 4 hr.; more concentrated hydrochloric acid (50 c.c.) was added after 2 hr. The hot solution was filtered, made strongly alkaline with 40% aqueous sodium hydroxide (320 g.), and saturated under pressure with hydrogen sulphide. The precipitate was centrifuged down and the supernatant solution was decanted off, adjusted to pH 6—7 with concentrated hydrochloric acid, and extracted with ether, to give crude *p*-(*NN*-di-2-hydroxyethylamino)thiophenol as a yellow oil (2·3 g., 29%) (Found: thiol-S, 12·0. Calc. for $C_{10}H_{15}O_2NS$: thiol-S, 15·05%). Reaction of a portion with chloro-2 : 4-dinitrobenzene in aqueous-ethanolic alkali gave p-(NN-*di*-2-*hydroxyethylamino*)*phenyl* 2 : 4-*dinitrophenyl sulphide*, orange-red prisms, m. p. 152—153° (from methanol) (Found: C, 50·7; H, 4·8; N, 10·8. $C_{16}H_{17}O_6N_3S$ requires C, 50·6; H, 4·5; N, 11·1%).

NN-*Di*-2′-*chloroethyl*-p-*thiocyanatoaniline*.—(i) *From* NN-*di*-2′-*hydroxyethyl*-p-*thiocyanatoaniline*. The diol (5 g.) was heated with phosphorus oxychloride (8 c.c.) on the steam-bath for 30 min. and the mixture was then cooled and poured into ice-water (100 c.c.). The solution was neutralised with saturated aqueous sodium hydrogen carbonate and extracted with benzene, to give an oil which was chromatographed in benzene on alumina to give *NN*-di-2′-chloroethyl-*p*-thiocyanatoaniline as a yellow oil (2·3 g., 39%), which did not crystallise but was characterised by reduction to the thiol (see below) and formation of the 2 : 4-dinitrophenyl sulphide, m. p. and mixed m. p. 155°.

(ii) *From* NN-*di*-2′-*chloroethylaniline* (with A. M. Creighton). A solution of bromine (14·7 g.) and sodium bromide (5 g.) in dry methanol (50 c.c.) was added (5—10 min.) to a stirred solution of *NN*-di-2′-chloroethylaniline (20 g.) and "AnalaR" ammonium thiocyanate (15·0 g.) in dry methanol (300 c.c.) at *ca.* 5°. Stirring was continued for a further 10 min., and the

mixture was then poured into water (1 l.) to precipitate NN-*di*-2′-*chloroethyl*-p-*thiocyanatoaniline* as a colourless solid (25·3 g., 100%), m. p. 40—41°. Recrystallisation from ethanol gave leaflets, m. p. 49° (Found: C, 48·1; H, 4·6; N, 9·9. $C_{11}H_{12}N_2SCl_2$ requires C, 48·0; H, 4·4; N, 10·2%).

The use of acetic acid in place of methanol gave a crude product which after chromatography on alumina gave the same material (74%), m. p. 47—48°.

p-(NN-*Di*-2-*chloroethylamino*)*thiophenol*.—(i) *From* NN-*di*-2′-*chloroethyl*-p-*thiocyanatoaniline*. The thiocyanate (27 g.) in anhydrous ether (300 c.c.) was added dropwise to a stirred suspension of finely powdered lithium aluminium hydride (3·0 g.) in anhydrous ether at such a rate (30 min.) as to maintain gentle reflux. The mixture was then stirred and refluxed for a further 30 min. (by which time the initial pale yellow colour of the solution had disappeared), then cooled before the excess of reagent was decomposed by ice-water. The precipitated complex was decomposed by ice-cold 6N-aqueous hydrochloric acid, the pH then brought to *ca.* 6 with saturated aqueous sodium hydrogen carbonate, the ether layer separated, and the aqueous solution re-extracted with ether (3 × 100 c.c.). The combined, dried (Na_2SO_4) extracts were evaporated under nitrogen to yield an oil which crystallised on trituration with a little methanol. The solid was washed with light petroleum (b. p. 40—60°) and dried *in vacuo* (22·4 g., 90%; m. p. 57—58°). p-(NN-*Di*-2′-*chloroethylamino*)*thiophenol* on recrystallisation from methanol formed pale cream prisms, m. p. 59—60° (Found: C, 47·8; H, 5·4; N, 5·4; thiol-S, 12·8. $C_{10}H_{13}NSCl_2$ requires C, 48·0; H, 5·2; N, 5·6; thiol-S, 12·8%). The crystalline thiol became blue-green when exposed to the air for a few hours; this occurred more rapidly when it was moistened with methanol or ethanol and was presumably due to oxidation.

Reaction of the thiol with chloro-2 : 4-dinitrobenzene in ethanol–benzene containing the theoretical amount of alkali gave p-(NN-*di*-2′-*chloroethylamino*)*phenyl* 2 : 4-*dinitrophenyl sulphide*, which crystallised from ethanol–benzene in orange-red prisms, m. p. 156—157° (Found: C, 46·5; H, 4·0; N, 10·1. $C_{16}H_{15}O_4N_3SCl_2$ requires C, 46·2; H, 3·6; N, 10·1%).

(ii) *From di*-[p-(NN-*di*-2-*chloroethylamino*)*phenyl*] *disulphide*. The disulphide (27·0 g.) in dry ether (250 c.c.) was reduced with lithium aluminium hydride (2·5 g.) in ether (200 c.c.), and the mixture worked up as described above for the reduction of the thiocyanate, except that refluxing was continued for 40 min. and 2N-hydrochloric acid was used to decompose the complex. The thiol was obtained as a waxy solid (26·7 g., 98%) (Found: thiol-S, 10·9%). It readily gave the 2 : 4-dinitrophenyl derivative described above, m. p. and mixed m. p. 156—157°.

p-(NN-*Di*-2-*chloroethylamino*)*phenyl Thiolacetate*.—A solution of *p*-(*NN*-di-2-chloroethylamino)thiophenol (6·0 g.) in acetic anhydride (35 c.c.) and pyridine (3 c.c.) was heated for 3 hr. on a steam-bath under nitrogen, then cooled and poured into water (800 c.c.). The precipitated solid on recrystallisation from ethanol (charcoal) gave the *thiolacetate*, pale yellow prisms (4·2 g., 60%), m. p. 63—64°, raised to 64—65° on further recrystallisation from ethanol (Found: C, 49·6; H, 5·4; Cl, 24·4. $C_{12}H_{15}ONSCl_2$ requires C, 49·3; H, 5·2; Cl, 24·3%).

p-(NN-*Di*-2-*chloroethylamino*)*phenyl Thiolbenzoate* (with A. M. Creighton).—A solution of *p*-(*NN*-di-2-chloroethylamino)thiophenol (5·0 g.) and benzoic anhydride (5·0 g.) in pyridine (30 c.c.) was set aside overnight and then diluted with water (100 c.c.). The precipitated solid, on recrystallisation from acetone–ethanol, gave the S-*benzoyl derivative*, pale yellow prisms (6·1 g., 86%), m. p. 109—110° (Found: C, 57·4; H, 5·1; Cl, 20·1. $C_{17}H_{17}ONSCl_2$ requires C, 57·6; H, 4·8; Cl, 20·0%).

NN-*Di*-2′-*chloroethyl*-p-(*methylthio*)*aniline*.—A solution of diazomethane (from 4 g. of α-nitrosomethylurea) in dry ether (35 c.c.) was added, with swirling, to *p*-(*NN*-di-2′-chloroethylamino)thiophenol (5·0 g.) in dry ether (20 c.c.). There was quiet effervescence until about three-quarters of the diazomethane had been added after which there was no apparent reaction. The mixture was kept at 0° overnight, then allowed to warm to room temperature; charcoal, moistened with concentrated hydrochloric acid, was added, and after the effervescence had ceased the mixture was shaken for 5 min., then neutralised with aqueous sodium hydrogen carbonate and filtered; the charcoal residue was washed with warm ether, and the aqueous phase extracted with ether. The combined ether solutions were dried (Na_2SO_4) and evaporated to a pasty solid which was chromatographed in benzene on alumina to give NN-*di*-2′-*chloroethyl*-p-(*methylthio*)*aniline* (1·8 g., 26%), m. p. 58—60° raised to 62—63° on recrystallisation (prisms, from methanol) (Found: C, 50·1; H, 5·95; Cl, 27·05. $C_{11}H_{15}NSCl_2$ requires C, 50·0; H, 5·7; Cl, 26·8%).

p-(NN-*Di*-2-*chloroethylamino*)*phenyl Thiolcarbamate*.—A solution of *NN*-di-2-chloroethyl-*p*-thiocyanatoaniline (2·8 g.) in ice-cold 94% sulphuric acid (28 c.c.) was kept overnight at 0°,

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then poured on crushed ice (300 g.). The precipitated solid was collected, washed with water (200 c.c.), and recrystallised from ethanol to give p-(NN-*di*-2-*chloroethylamino*)*phenyl thiolcarbamate* as pale yellow prisms (1·53 g., 52%), m. p. 158° (Found: C, 45·1; H, 5·0; N, 9·3. $C_{11}H_{14}ON_2SCl_2$ requires C, 45·05; H, 4·8; N, 9·55%).

p-(NN-*Di*-2-*chloroethylamino*)*phenyl* N-*Phenylthiolcarbamate*.—Phenyl *iso*cyanate (0·61 g.) and *p*-(*NN*-di-2-chloroethylamino)thiophenol (1·25 g.) were heated together in a sealed tube at 100° for 3 hr. and then set aside overnight. The solid product on recrystallisation from acetone–ethanol gave p-(NN-*di*-2-*chloroethylamino*)*phenyl* N-*phenylthiolcarbamate* (1·03 g., 56%), m. p. 143°, raised to 146—147° on recrystallisation from ethanol (Found: C, 55·4; H, 5·2; N, 7·35. $C_{17}H_{18}ON_2SCl_2$ requires C, 55·3; H, 4·9; N, 7·6%).

p-(NN-*Di*-2-*chloroethylamino*)*phenyl* 2 : 3 : 4 : 6-*Tetra*-O-*acetyl*-β-D-*thioglucoside*.—α-Acetobromoglucose (8·22 g.) was added to a solution of *p*-(*NN*-di-2-chloroethylamino)thiophenol (5·63 g.) and potassium hydroxide (1·10 g.) in chloroform–ethanol (1 : 2) (90 c.c.). The solution was refluxed for 30 min., then cooled and washed with water; the chloroform layer was removed and the aqueous phase was re-extracted with chloroform. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and with water, dried (Na_2SO_4), and concentrated to give a solid (7·2 g., 62%), m. p. 110—112°. Recrystallisation from ethanol gave p-(NN-*di*-2-*chloroethylamino*)*phenyl* 2 : 3 : 4 : 6-*tetra*-O-*acetyl*-β-D-*thioglucoside*, colourless needles, m. p. 110—111°, $[\alpha]_D^{22}$ −44° (*c* 2 in $CHCl_3$) (Found: C, 49·7; H, 5·4; Cl, 12·1. $C_{24}H_{31}O_9NSCl_2$ requires C, 49·7; H, 5·4; Cl, 12·2%).

p-(NN-*Di*-2-*chloroethylamino*)*phenyl* β-D-*Thioglucoside*.—The above tetra-acetate (2·02 g.) was suspended in anhydrous methanol, and a small piece of sodium (*ca.* 5 mg.) was added. The flask was sealed, swirled until all the solid had dissolved, and then kept overnight at 0°. The solution was neutralised with carbon dioxide and evaporated to an oil which on crystallisation from ethanol–pentane gave p-(NN-*di*-2-*chloroethylamino*)*phenyl* β-D-*thioglucoside*, needles, (1·09 g., 76%), m. p. 85—87°, $[\alpha]_D^{22}$ −40° (*c* 2 in pyridine) (Found: C, 46·8; H, 5·7; Cl, 17·4. $C_{16}H_{23}O_5NSCl_2$ requires C, 46·6; H, 5·6; Cl, 17·2%).

Methyl Ester of S-p-(NN-*Di*-2-*chloroethylamino*)*phenyl* 2 : 3 : 4-*Tri*-O-*acetyl*-β-D-*thioglucuronic Acid*.—Potassium (0·80 g.) was dissolved in anhydrous methanol (175 c.c.), *p*-(*NN*-di-2-chloroethylamino)thiophenol (5·50 g.) was added, the air in the flask was displaced with nitrogen, and the solution was warmed to dissolve the thiophenol and then cooled to 0°. Methyl α-acetobromoglucuronate [28] (8·20 g.) was added, and the mixture was shaken, with continued cooling, until all the acetobromo-sugar had dissolved. The solution was kept at 0° for 20 min. and then allowed to warm to room temperature; it had then become neutral. It was filtered and concentrated under reduced pressure to an oil, which was dissolved in chloroform (100 c.c.), washed with saturated aqueous sodium hydrogen carbonate, and recovered. It was then dissolved in pyridine (25 c.c.) and acetic anhydride (25 c.c.), kept at 0° overnight, poured into water (400 c.c.), stirred for 10 min., then acidified with 2N-sulphuric acid (200 c.c.), and extracted with chloroform to give an oil. On crystallisation from methanol this gave the *thioglucuronate*, colourless prisms (6·79 g., 55%), m. p. 134—136°, $[\alpha]_D^{25}$ −43° (*c* 2 in $CHCl_3$) (Found: C, 48·85; H, 5·35; Cl, 13·0. $C_{23}H_{29}O_9NSCl_2$ requires C, 48·8; H, 5·2; Cl, 12·5%).

Cholest-5-en-3β-yl p-(NN-*Di*-2-*chloroethylamino*)*phenyl Disulphide*.—3β-Mercaptocholest-5-ene [29] (4·83 g.) in dry benzene (30 c.c.) was added dropwise with stirring to a solution of *N*-chlorosuccinimide (1·60 g.) in dry benzene (100 c.c.) at 5—8°, with exclusion of light and moisture. Stirring was continued for 15 min. after addition was complete, and the mixture was allowed to attain room temperature before being filtered to remove succinimide (0·9 g.; m. p. 124—126°). A solution of *p*-(*NN*-di-2-chloroethylamino)thiophenol (3·0 g.) in dry benzene (10 c.c.) was then added. A reaction occurred and hydrogen chloride was evolved; a pasty solid, presumably a mixture of hydrochlorides, separated. The mixture was heated to 50—60° for 10 min., then cooled, washed with saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated under reduced pressure to an oil, which was chromatographed on alumina (6 cm. × 30 cm.) with benzene–light petroleum (b. p. 60—80°) (1 : 1) as eluant.

The initial colourless eluates (1·25 l.) yielded di-(cholest-5-en-3β-yl) disulphide, which crystallised from acetone in pearly leaflets (2·1 g.), m. p. 143—144° (lit.,[30] m. p. 144·5°). The

[28] Bollenback, Long, Benjamin, and Lindquist, *J. Amer. Chem. Soc.*, 1955, **77**, 3310.
[29] O'Connor and Nace, *J. Amer. Chem. Soc.*, 1953, **75**, 2118.
[30] Wagner-Jauregg and Lennartz, *Ber.*, 1941, **74**, 27.

very pale yellow eluates (500 c.c.) that followed yielded an oil, a solution of which in propan-2-ol–ether slowly deposited colourless crystals of *cholest-5-en-3β-yl* p-(NN-*di*-2-*chloroethylamino*)-*phenyl disulphide* (2·02 g., 26%), m. p. 71—72°, $[\alpha]_D^{25}$ −36° (*c* 2 in $CHCl_3$) (Found: C, 68·2; H, 8·9; Cl, 11·2. $C_{37}H_{57}NS_2Cl_2$ requires C, 68·3; H, 8·8; Cl, 10·9%). A further small quantity of the mixed disulphide (0·5 g.) was obtained from the next eluates (500 c.c.).

Elution of the residual slowly moving yellow band gave di-[*p*-(*NN*-di-2-chloroethylamino)-phenyl] disulphide (1·4 g., 46%), m. p. 75—76° after recrystallisation from ethanol.

2 : 3 : 4 : 6-*Tetra*-O-*acetyl*-β-D-*thioglucose*.—Prepared in 79% yield by Schneider and Bansa's method,[31] this initially had m. p. 70—72°, but m. p. 112—113° after being kept for 6 months under nitrogen at room temperature. A second preparation had m. p. 116—117°, undepressed with the previous sample (m. p. 112—113°). Wrede [32] gives m. p. 75°, Richtmyer *et al.*[33] 74—75°, Schneider and Bansa [31] 113—114°.

p-(NN-*Di*-2-*chloroethylamino*)*phenyl* 2 : 3 : 4 : 6-*Tetra*-O-*acetyl*-β-D-*glucosyl Disulphide*.—2 : 3 : 4 : 6-Tetra-*O*-acetyl-β-D-thioglucose (3·64 g.) in dry benzene (50 c.c.) was added dropwise to a cold (10—12°), stirred, suspension of *N*-bromosuccinimide (1·78 g.) in dry benzene (100 c.c.), with exclusion of light and moisture. The mixture was stirred for a further 10 min., then filtered from succinimide. *p*-(*NN*-Di-2-chloroethylamino)thiophenol (2·50 g.) in dry benzene (10 c.c.) was added to the solution; there was an immediate reaction, with evolution of hydrogen bromide and precipitation of a yellow, sticky paste. The mixture was warmed to 60° for 10 min. and then cooled; the supernatant liquid was decanted off from the pasty solid {which from its yellow colour was judged to be mainly the hydrobromide of di-[*p*-(*NN*-di-2-chloroethyl-amino)phenyl] disulphide}, washed with saturated sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated to an oil, which on crystallisation from ethanol gave the mixed *disulphide* (2·63 g., 43%), m. p. 100—102°, $[\alpha]_D^{22}$ −273° (*c* 2 in $CHCl_3$) (Found: C, 47·4; H, 5·4; Cl, 11·2. $C_{24}H_{31}O_9NS_2Cl_2$ requires C, 47·1; H, 5·1; Cl, 11·6%).

The yellow solid remaining after decantation of the benzene solution was triturated with benzene and saturated sodium hydrogen carbonate. The benzene layer furnished di-[*p*-(*NN*-di-2-chloroethylamino)phenyl] disulphide, m. p. 76° (from ethanol).

NN-*Di*-2′-*bromoethylaniline*.—Phosphorus pentabromide (86 g.) was added in small portions to a solution of *NN*-di-2′-hydroxyethylaniline (30 g.) in chloroform (150 c.c.), the vigour of the reaction being controlled by external cooling. The homogeneous solution was then refluxed for 30 min. (colourless needles, possibly of a hydrobromide, separated after about 20 min.), cooled, stirred with ice-water (600 c.c.), and neutralised by the cautious addition of solid sodium hydrogen carbonate. The aqueous phase was re-extracted with chloroform and the combined extracts were dried (Na_2SO_4) and evaporated to an oil, which was distilled (b. p. 136—138°/1 mm.). The distillate solidified (m. p. 50—52°), and on recrystallisation from light petroleum (b. p. 40—60°) gave colourless prisms (41 g., 80%), m. p. 53—54° (lit.,[10] m. p. 53—55°).

NN-*Di*-2′-*bromoethyl*-p-*thiocyanatoaniline* (with A. M. CREIGHTON).—A stirred solution of *NN*-di-2′-bromoethylaniline (30 g.) and ammonium thiocyanate (16 g.) in dry methanol (650 c.c.) was treated, as described for the chloro-analogue, with bromine (15·7 g.) and sodium bromide (8 g.) in methanol (80 c.c.). The mixture was stirred for a further 20 min. and then poured into water. NN-*Di*-2′-*bromoethyl*-p-*thiocyanatoaniline* was precipitated as a colourless solid (33·8 g., 95%), m. p. 64—65°; recrystallisation of a portion from ethanol gave needles, m. p. 68° (Found: C, 36·5; H, 3·65; N, 7·4. $C_{11}H_{12}N_2SBr_2$ requires C, 36·3; H, 3·3; N, 7·7%).

p-(NN-*Di*-2-*bromoethylamino*)*phenyl Thiolcarbamate*.—Controlled hydrolysis of *NN*-di-2-bromoethyl-*p*-thiocyanatoaniline (2 g.) with 95% ice-cold sulphuric acid, as described for the chloro-compound, gave p-(NN-*di*-2-*bromoethylamino*)*phenyl thiolcarbamate*, platelets (from benzene) (1·8 g., 85%), m. p. 165—166° (Found: C, 34·7; H, 3·9; N, 6·95. $C_{11}H_{14}ON_2SBr_2$ requires C, 34·6; H, 3·7; N, 7·3%).

p-(NN-*Di*-2-*bromoethylamino*)*thiophenol* (with A. M. CREIGHTON).—*NN*-Di-2-bromoethyl-*p*-thiocyanatoaniline (10·0 g.) in warm ether (200 c.c.) was reduced by addition to a suspension of lithium aluminium hydride (1·0 g.) in ether (100 c.c.), and the product isolated, as described for the reduction of the chloro-compound. Recrystallisation from ethanol–light petroleum

[31] Schneider and Bansa, *Ber.*, 1931, **64**, 1321.
[32] Wrede, *Z. physiol. Chem.*, 1922, **119**, 46.
[33] Richtmyer, Carr, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 1477.

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(b. p. 40—60°) gave almost colourless prisms of p-(NN-*di*-2-*bromoethylamino*)*thiophenol* (8·95 g., 95%), m. p. 84—86°, raised to 88—89° on recrystallisation from ethanol (Found: C, 36·0; H, 4·1; Br, 47·4; thiol-S, 9·3. $C_{10}H_{13}NSBr_2$ requires C, 35·4; H, 3·9; Br, 47·4; thiol-S, 9·5%). It became blue-green on exposure to air. Reaction of the thiol with chloro-2 : 4-dinitrobenzene failed to give a satisfactory derivative.

Di-[p-(NN-*di*-2-*bromoethylamino*)*phenyl*] *Disulphide*.—*p*-(*NN*-Di-2-bromoethylamino)thiophenol (2·0 g.) was oxidised with iodine as described for the chloro-compound. The product, after chromatography and recrystallisation from acetone–ethanol, gave the *disulphide* (1·4 g., 71%), m. p. 78—79° (Found: C, 36·0; H, 3·95; Br, 47·1. $C_{20}H_{24}N_2S_2Br_4$ requires C, 35·5; H, 3·6; Br, 47·3%).

NN-*Di*-2′-*bromoethyl*-4-(*methylthio*)*aniline*.—*p*-(*NN*-Di-2-bromoethylamino)thiophenol (4·0 g.) in dry ether (50 c.c.) was treated with diazomethane (from 4·0 g. of α-nitrosomethylurea) in dry ether, and the product isolated as described for the chloro-compound. The S-*methyl derivative* was obtained as colourless prisms (1·27 g., 30%), m. p. 57° (from ethanol) (Found: C, 37·5; H, 3·5; Br, 45·8. $C_{11}H_{15}NSBr_2$ requires C, 37·4; H, 4·3; Br, 45·3%).

p-(NN-*Diethylamino*)*thiophenol*.—*NN*-Diethyl-*p*-thiocyanatoaniline, b. p. 145°/0·5 mm. (lit.,[34] b. p. 138°/1 mm.), was prepared from *NN*-diethylaniline by the method [35] described for the *NN*-dimethyl compound. It was reduced with lithium aluminium hydride, as described above for the di-2′-chloroethyl analogue, to *p*-(*NN*-diethylamino)thiophenol (50—70%), b. p. 97—98°/0·06 mm., 124°/0·14 mm., n_D^{20} 1·5942. No physical constants were recorded by Montgomery *et al.*[23]

Reaction of the thiol with chloro-2 : 4-dinitrobenzene in aqueous alkaline ethanol gave p-NN-*diethylaminophenyl* 2 : 4-*dinitrophenyl sulphide*, orange-red plates (from ethyl acetate), m. p. 147° (Found: C, 55·6; H, 5·0; N, 11·9. $C_{16}H_{17}O_4N_3S$ requires C, 55·3; H, 4·9; N, 12·1%).

Acetylation of the thiol with acetic anhydride and a trace of sulphuric acid for 30 min. at 100° gave the S-*acetyl derivative* (3·5 g., 71%), b. p. 152—153°/0·75 mm., n_D^{21} 1·5920 (Found: C, 64·4; H, 7·9; N, 6·2. $C_{12}H_{17}ONS$ requires C, 64·55; H, 7·7; N, 6·3%).

Oxidation of the thiol with iodine, as described for the di-2′-chloroethyl analogue gave the disulphide, which crystallised from ethanol in yellow prisms, m. p. 74°. Holzmann [14] gives m. p. 69—72° for the product obtained by reaction of sulphur monochloride with diethylaniline.

Mixed Disulphides Derived from 2 : 4-*Dinitrobenzenesulphenyl Chloride* (with A. M. Creighton).—A solution of *p*-(*NN*-di-2-bromoethylamino)thiophenol (2·6 g.) in dry benzene (30 c.c.) was added slowly to 2 : 4-dinitrobenzenesulphenyl chloride [36] (1·8 g.) in dry benzene (30 c.c.). The mixture was shaken for a few minutes and set aside overnight. It was then poured into saturated aqueous sodium hydrogen carbonate (150 c.c.), the benzene layer was removed, washed with water, dried, and concentrated, and the residue transferred to a column of alumina. Elution with benzene gave p-(NN-*di*-2-*bromoethylamino*)*phenyl* 2 : 4-*dinitrophenyl disulphide* as golden-yellow needles (2·4 g.), m. p. 119—120°, transformed by recrystallisation from acetone–ethanol into deep red prisms (2·1 g.), m. p. 132—133° (a mixture of the two forms had m. p. 132—133°) (Found: C, 35·9; H, 3·0; N, 7·9. $C_{16}H_{15}O_4N_3S_2Br_2$ requires C, 35·8; H, 2·8; N, 7·8%).

Prepared in a similar way p-(NN-*di*-2-*chloroethylamino*)*phenyl* 2 : 4-*dinitrophenyl disulphide* formed red prisms, m. p. 140° (from acetone–ethanol) (Found: C, 43·0; H, 3·8; N, 9·3. $C_{16}H_{15}O_4N_3S_2Cl_2$ requires C, 42·9; H, 3·4; N, 9·4%); and p-NN-*diethylaminophenyl* 2 : 4-*dinitrophenyl disulphide* formed purple prisms, m. p. 109° (from acetone–ethanol) (Found: C, 50·8; H, 4·9; N, 11·0. $C_{16}H_{17}O_4N_3S_2$ requires C, 50·6; H, 4·9; N, 11·1%).

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[34] Fichter and Schonmann, *Helv. Chim. Acta*, 1936, **19**, 1411.
[35] *Org. Syntheses*, Coll. Vol. II, p. 574.
[36] Kharasch, Gleason, and Buess, *J. Amer. Chem. Soc.*, 1950, **72**, 1796.

572. *Hexamethyl Compounds of Silicon, Germanium, and Tin.*

By M. P. Brown and G. W. A. Fowles.

Hexamethyldisilane, hexamethyldigermane, and hexamethyldistannane have been prepared, the germanium compound for the first time. The conditions for preparation of hexamethyldisilane from trimethylchlorosilane have been systematically studied. Whereas the hexamethyl compounds of silicon and germanium are not cleaved by solutions of sodium–potassium alloy in ethylene glycol dimethyl ether, hexamethyldistannane gives the potassium salt of trimethyltin.

Carbon, silicon, germanium, tin, and lead form compounds $(R_3M)_2$, where R is alkyl or aryl. Whereas the hexa-aryl compounds have been studied in some detail by Gilman and his co-workers (1953—57),[1] little systematic work has been reported for the hexa-alkyls since the investigations by Kraus *et al.* (1925—34).[2,3,4] As we wished to study the metal–metal bonds through the Raman and infrared spectra of the hexamethyl compounds (to be published), we prepared and examined the silicon, germanium, and tin compounds.

The most important general preparative method, the reduction of the appropriate trialkylhalogeno-compound by an alkali metal, is best carried out in liquid ammonia with tin compounds, and in this solvent we have repeated Kraus and Sessions's [2] preparation of hexamethyldistannane. Since silicon– and germanium–halogen bonds are readily ammonolysed, the hexa-alkyl compounds of these elements cannot be prepared in liquid ammonia, and the trialkylhalogeno-compound is usually reduced by refluxing it with the alkali metal, sometimes in an inert solvent. Hexamethyldigermane was obtained in good yield by the reduction of trimethylbromogermane by molten potassium. As hexamethyldisilane had been made, until recently, only by the reaction of hexahalogenodisilanes with organometallic compounds,[5] we studied the reduction of trimethylchlorosilane. Although the results of a study of the analogous reduction of trimethyliodosilane [6] are now available, in view of the greater availability of the chloro-compound we extended our study in order to find the best method for preparing hexamethyldisilane. Results are shown in the Table.

Reaction of trimethylchlorosilane with alkali metals.

Alkali metal	Solvent	(ml.)	Me_3SiCl (ml.)	Reflux time (hr.)	Yield of Me_6Si_2 (%) *
Li (solid)	None		10	2·5	0
Li (solid)	Di-*n*-butyl ether	(10)	10	2·5	0
Na (liquid)	None		10	24 †	0
Na (solid)	Tetrahydrofuran	(50)	10	12	0
Na (liquid)	Xylene	(200)	30	12	0
K (liquid)	None		10	24	92
K (liquid)	Tetrahydrofuran	(20)	10	3	50
K (liquid)	Ethylene glycol dimethyl ether	(80)	20	3	59
Na/K (liquid)	Ethylene glycol dimethyl ether	(15)	3	2 ‡	43

* 0 = No reaction. † In a sealed tube at 120°. ‡ At room temperature.

Although trimethyliodosilane,[6] trimethylbromosilane,[4] and triethylchlorosilane [7] can be reduced by molten sodium, trimethylchlorosilane did not react even in boiling xylene, yet molten potassium readily reduced it; in the presence of tetrahydrofuran or ethylene glycol dimethyl ether yields were somewhat lower, partly because of the difficulty in

[1] Gilman and Gerow, *J. Org. Chem.*, 1957, **22**, 334. This paper, which describes triphenylgermyltriphenyltin, is the latest of the series on hexaphenyl compounds.
[2] Kraus and Sessions, *J. Amer. Chem. Soc.*, 1925, **47**, 2361.
[3] Kraus and Flood, *J. Amer. Chem. Soc.*, 1932, **54**, 1635.
[4] Kraus and Nelson, *J. Amer. Chem. Soc.*, 1934, **56**, 195.
[5] Brockway and Davidson, *J. Amer. Chem. Soc.*, 1941, **63**, 3287.
[6] Voronkov and Khudobin, *Zhur. obshchei Khim.*, 1956, **26**, 584.
[7] Gilman, Ingham, and Smith, *J. Org. Chem.*, 1953, **18**, 1743.

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" working up " and possibly owing to solvolysis of the trimethylchlorosilane.[6] Potassium probably forms transient solutions which react immediately with trimethylchlorosilane, since both potassium and sodium–potassium alloy [8] (but not lithium or sodium) form fairly stable, blue, diamagnetic solutions in this ether, analogous to those formed by alkali metals in amines.[9] Trimethylchlorosilane was rapidly reduced by these metal solutions, and although the blue colour disappeared throughout the solvent, reaction continued at the metal surface. Unlike reductions in liquid ammonia, the effects of solvolysis did not appear to be important.

In all successful reductions of trimethylchlorosilane and trimethylbromogermane, the potassium halide was dark blue, presumably because of colloidal particles of excess of alkali metal or *F* centres in the halide crystals.[10]

Properties of the Hexamethyl Compounds.—The simple physical properties show, as expected, a greater change between germanium and tin than between silicon and germanium: Si_2Me_6: m. p. 12°, b. p. 113°/760 mm., n_D^{20} 1·4224; Ge_2Me_6: m. p. −40°, b. p. 138°/750 mm., n_D^{20} 1·4564; Sn_2Me_6: m. p. 23°, b. p. 182°/756 mm. The silicon and germanium compounds are colourless liquids with pleasant fruity smells, which can be distilled in air and do not react appreciably with cold concentrated sulphuric acid. Kumada [17] *et al.* have, however, shown that prolonged stirring with concentrated sulphuric acid leads to the ionisation of a silicon–carbon bond. Hexamethyldistannane has an unpleasant smell, and reacts slowly with oxygen at room temperature to form bis(trimethyltin) oxide.

Hexa-aryl compounds of all the Group IVB elements [11,12] and hexa-alkyl compounds of tin and lead can be split by alkali metals to give the alkali-metal salts, *e.g.*, $Ph_6Si_2 + 2K = 2Ph_3SiK$. Hexa-alkyl compounds of silicon and germanium are more resistant, however; thus hexaethyldisilane is not split by solutions of sodium in liquid ammonia, by lithium in ethylamine,[4] or by sodium–potassium alloy (either alone or with a number of ethers); hexaethyldigermane is not split by metal–ammonia solutions although some reaction appears to take place with solutions of lithium and potassium in ethylamine.[3]

Since the non-reduction of the hexa-alkyl compounds of silicon and germanium by metal–ammonia solutions might be attributed in part to their insolubility in liquid ammonia, we attempted the reduction with solutions of sodium–potassium alloy in ethylene glycol dimethyl ether (in which the hexamethyl compounds are soluble). Substantial amounts of the hexamethyls could be recovered even after three days, and the yellow colour expected [18] if potassium salts were formed did not appear. Hexamethyldigermane was not, moreover, reduced when refluxed with potassium. It seems, therefore, that the silicon–silicon and germanium–germanium bonds in the hexamethyl compounds are truly resistant to reduction by alkali metals. Gilman [18] has shown that reduction becomes possible when methyl groups are replaced by phenyl groups; thus 1 : 1 : 2 : 2-tetramethyl-1 : 2-diphenyldisilane reacts slowly with lithium in tetrahydrofuran, whereas 1 : 2-dimethyl-1 : 1 : 2 : 2-tetraphenyldisilane reacts immediately.

In contrast to the stability of the silicon–silicon and germanium–germanium bonds, the tin–tin bond is easily cleaved; hexamethyldistannane reacts immediately with alloy solutions in ethylene glycol dimethyl ether to give potassium trimethyltin; this salt with tri-*p*-tolylbromostannane gave 1 : 1 : 1-trimethyl-2 : 2 : 2-tri-*p*-tolyldistannane.

Metal–metal bonds in the hexa-alkyl and hexa-aryl compounds are cleaved both with metal solutions and with the metal in an inert solvent. When the metal is in solution, we can consider it to be dissociated completely into metal ions and (solvated) electrons [9] (single or paired), $M \longrightarrow M^+ + e$, and it seems reasonable to consider the reduction to

[8] Down, Lewis, Moore, and Wilkinson, *Proc. Chem. Soc.*, 1957, 209.
[9] Fowles, McGregor, and Symons, *J.*, 1957, 3329.
[10] Seitz, *Rev. Mod. Phys.*, 1954, **26**, 7.
[11] Gilman and Dunn, *Chem. Rev.*, 1953, **52**, 94.
[12] Brook and Gilman, *J. Amer. Chem. Soc.*, 1954, **76**, 278.

be caused by these electrons, $R_3M{-}MR_3 + 2e \longrightarrow 2R_3M^-$. From the low ionisation potentials of the alkali metals, we might expect that the first stage of the reduction by the metal in an inert solvent would be the ionisation of the metal atoms, followed by the interaction of the electron with the hexa-alkyl compound.

As the atomic weight of M increases, so the M–M bond in the R_6M_2 compounds gets weaker and longer, and should accordingly break more easily. It is not surprising therefore that hexamethyldistannane is cleaved whereas the analogous germanium and silicon compounds are inert. When the methyl groups are replaced by phenyl groups, the M–M bond should weaken because of the greater electron-withdrawing power of the phenyl groups. The M–M bonds become more vulnerable to attack by the electrons. Moreover, the triarylmetal anions formed in the reaction will be appreciably stabilised by delocalisation of the negative charge on to the three phenyl groups.

Experimental

Analysis.—Silicon, germanium, and tin were estimated by dry combustion.[13]

Materials.—Solvents were fractionated and dried. Germanium(IV) bromide was prepared [14] from bromine vapour and germanium metal at 400°. Tetramethylgermane was obtained in 75% yield from germanium(IV) bromide and methylmagnesium iodide in di-*n*-butyl ether.[15] Trimethylbromogermane was prepared in 85% yield by keeping tetramethylgermane and bromine (*ca.* 0·2 mol. excess) in a sealed tube for a week, followed by fractionation.[16] Trimethylbromostannane was prepared and purified by Kraus's method.[2]

Tri-*p*-tolylchlorostannane, prepared from tin(IV) chloride and tetra-*p*-tolylstannane, was hydrolysed to the hydroxide, and then converted into the bromo-analogue with hydrobromic acid.

Solutions of sodium–potassium alloy in ethylene glycol dimethyl ether were made by melting the metals together *in vacuo* and distilling on the freshly dried ($LiAlH_4$) ether. These blue solutions were shown by paramagnetic resonance measurements [9] to be diamagnetic. Solutions of potassium metal could also be made, but lithium and sodium alone did not dissolve.

1. *Preparation of Hexamethyldisilane.*—(a) *Refluxing of trimethylchlorosilane with potassium and ethylene glycol dimethyl ether.* Trimethylchlorosilane (99%, Messrs. Hopkin and Williams) (0·78 mole) and potassium (0·86 g.-atom) were added, in portions of about 0·2 mole each, to the ether (200 ml.), and the mixture was refluxed under nitrogen for 6 hr. Volatile constituents were condensed *sub vacuo* into another flask and shaken with water, and then with cold concentrated sulphuric acid. The immiscible layer of hexamethyldisilane was washed with water, dried ($CaSO_4$), and fractionated to give a product with b. p. 113·1°/750 mm. and n_D^{20} 1·4224 [6] (Found: Si, 38·35, 38·24. Calc. for $C_6H_{18}Si_2$: Si, 38·38%). Reactions were carried out with other solvents (cf. Table) similarly.

(b) *Reaction of sodium and trimethylchlorosilane in a sealed tube.* Trimethylchlorosilane (1 mol.) and sodium (1 mol.) were heated in a sealed tube at 120° for 24 hr. The surface of the sodium became brown, but no hexamethyldisilane was isolated when the reaction mixture was worked up as in 1(a).

(c) *Reaction of trimethylchlorosilane with a solution of sodium–potassium alloy in ethylene glycol dimethyl ether.* The alloy (0·046 mole) was filtered *in vacuo* through a glass sinter to remove oxide into a tube made from an extended B14 joint, and the ether (15 ml.) and trimethylchlorosilane (0·023 mole) were condensed successively into the lower and upper parts of the tube; this was then sealed off *sub vacuo*. As the ether melted, the alloy dissolved to give a blue solution, but the colour disappeared as the trimethylchlorosilane melted and ran into it. After being shaken for 2 hr., the tube was opened under nitrogen, and the colourless volatile liquid was distilled from the blue-black solid and worked up as in experiment 1(a) to give hexamethyldisilane (43%).

2. *Preparation of Hexamethyldigermane by Refluxing of Trimethylbromogermane with*

[13] Brown and Fowles, *Analyt. Chem.*, in the press.
[14] Dennis and Hance, *J. Amer. Chem. Soc.*, 1922, **44**, 299.
[15] Lippincott and Tobin, *J. Amer. Chem. Soc.*, 1953, **75**, 4141.
[16] Dennis and Patnode, *J. Amer. Chem. Soc.*, 1930, **52**, 2779.

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Potassium.—This reaction was carried out on the vacuum line. Potassium (0·115 g.-atom) was filtered (sinter) into the reaction flask; trimethylbromogermane (0·092 mole) was condensed in and refluxed with the potassium in nitrogen. The voluminous potassium bromide formed hindered the reaction, and so the volatile material was several times condensed on fresh potassium. Unchanged trimethylbromogermane was removed by bubbling ammonia through the product and filtering off the white complex formed. The filtrate consisted of pure *hexamethyldigermane* (0·034 mole, 74%) distilling at 137°/772 mm., n_D^{25} 1·4564 (Found: Ge, 61·41, 61·37. $C_6H_{18}Ge_2$ requires Ge, 61·67%). It did not react when refluxed with potassium or shaken with cold concentrated sulphuric acid.

3. *Hexamethyldistannane.*—Trimethylbromostannane was reduced by sodium in liquid ammonia by Kraus and Sessions's [2] method; the hexamethyldistannane was recrystallised *in vacuo* from light petroleum (b. p. 60—80°) at −78°. The average yield of once-recrystallised hexamethyldistannane (m. p. 23°) was 71% (Found: Sn, 71·23, 71·48. Calc. for $C_6H_{18}Sn_2$: Sn, 72·46%).

4. *Action of Solutions of Sodium–Potassium Alloy in Ethylene Glycol Dimethyl Ether on the Hexamethyl Compounds.*—These experiments were carried out *in vacuo* in a similar apparatus to that used for experiment 1(c).

(a) *Hexamethyldisilane.* Sodium–potassium alloy, the ether (15 ml.), and hexamethyldisilane (1 ml.) were condensed into the reaction tube, which was then sealed. The blue colour of the alloy–ether solution faded as it touched the melting disilane, but the colour returned immediately when the tube was shaken. After intermittent shaking for three days, the tube was opened, and the volatile materials were removed and worked up as usual to give unchanged hexamethyldisilane (0·75 ml., b. p. 112°). A trace of white solid remained with the alloy, formed probably by the known reaction of the alloy with the ether.

(b) *Hexamethyldigermane.* This (0·9 g.) behaved similarly to hexamethyldisilane, although the blue colour of the alloy solution disappeared more quickly. After intermittent shaking for three days—a blue solution still formed, and was stable for about 5 min.—the tube was opened and the volatile materials were worked up as in (a) to give unchanged hexamethyldigermane (0·4 g.).

(c) *Hexamethyldistannane.* This (0·0094 mole) reacted immediately at room temperature to give a greenish-yellow solution. After being shaken for 10 min. the tube was opened under nitrogen and the contents filtered into tri-*p*-tolylbromostannane (0·0187 mole); the greenish-yellow colour disappeared on shaking. After removal of the volatile materials, extraction of the residue with light petroleum gave crystals of 1 : 1 : 1-*trimethyl*-2 : 2 : 2-*tri*-p-*tolyldistannane* (0·0051 mole, 38%), m. p. 139·5—141° (Found: Sn, 42·74, 43·01. $C_{24}H_{30}Sn_2$ requires Sn, 42·30%). Further extraction of the residue with toluene gave hexa-*p*-tolyldistannane (0·0023 mole, 25%), m. p. 251—252° (Found: Sn, 30·0, 30·2. Calc. for $C_{42}H_{42}Sn_2$: Sn, 30·27%).

(5) *Hexa*-p-*tolyldistannane.*—Tri-*p*-tolylbromostannane (0·0042 mole) was allowed to react with a solution of sodium–potassium alloy in ethylene glycol dimethyl ether; excess of alloy was removed by amalgamation with mercury. The mixture was filtered, and extraction of the residue with benzene gave crystals of hexa-*p*-tolyldistannane (0·00094 mole, 45%) (Found: Sn, 30·1%), m. p. undepressed on admixture with the product formed in reaction 4(c).

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THE UNIVERSITY, SOUTHAMPTON. [*Received, March 6th*, 1958.]

[17] Kumada *et al.*, *J. Org. Chem.*, 1956, **21**, 1264.
[18] Gilman, *J. Amer. Chem. Soc.*, 1958, **80**, 608.

573. *New* NN′-*Disubstituted Thioureas and Ureas of Biological Interest.*

By Ng. Ph. Buu-Hoï, Ng. D. Xuong, and (Miss) V. T. Suu.

The reactivity of several classes of aromatic and heterocyclic amines towards aryl *iso*cyanates and *iso*thiocyanates has been investigated, and a large number of new *NN′*-diaryl-thioureas and -ureas and their heterocyclic analogues, most of them bearing halogen groups, have been prepared for testing as potential antiviral and antibacterial agents.

Compounds possessing notable activity *in vivo* against influenza virus have been found in the group of fluorine-containing thiocarbanilides and analogous sulphur compounds;[1] numerous *pp′*-disubstituted thiocarbanilides possess pronounced antitubercular and fungistatic activity,[2] and some are active against human leprosy.[3] A large number of new *NN′*-diarylthioureas and their pyridine analogues, most of them bearing halogen substituents (particularly fluorine), have therefore been synthesised, by condensation of primary amines with aryl *iso*thiocyanates.[4] Other substituents included alkyl, alkyloxy-, and *NN*-dialkyl groups, whose favourable influence on tuberculostatic activity is known, and *cyclo*hexyl radicals, which have not previously been investigated but now prove likewise favourable. Among the pyridine compounds, *N*-(5-chloro-2-pyridyl)-*N′*-(*p*-fluorophenyl)thiourea is a heterocyclic analogue of 4-chloro-4′-fluorothiocarbanilide, the most active antiviral compound in the series. Condensations with aryl *iso*cyanates furnished *NN′*-diarylureas, also of interest in view of the pronounced activity of certain polychlorinated carbanilides towards *Micrococcus pyogenes* var. *aureus*;[5] *N*-(5-chloro-2-pyridyl)-*N′*-3 : 4-dichlorophenylurea is a heterocyclic analogue of 3 : 4 : 4′-trichlorocarbanilide, the most active staphylostatic compound in the aromatic series.

In these condensations, the greater chemical activity of aryl *iso*cyanates than of the corresponding *iso*thiocyanates was shown by exothermic formation of ureas in the cold, whereas preparation of most of the thioureas required slight heating; also by the ready formation of ureas from complex amines such as ketones bearing nuclear amino-groups (*e.g.*, 4-amino-acetophenone and -benzophenone), methyl homologues of 2-aminopyrimidine, and 2-amino-5-nitrothiazole, all of which failed to give the corresponding thioureas under the same conditions. Similarly, sterically hindered arylamines such as *o*-trifluoromethylaniline reacted instantaneously with aryl *iso*cyanates, but sluggishly or not at all with aryl *iso*thiocyanates.[6] The new symmetrical *NN′*-diarylthioureas reported were prepared from the corresponding arylamines and carbon disulphide, by the Hugershoff method.[7]

The arylamines used in this work were characterised by various other reactions, including the formation of 2-arylamino-3-chloro-1 : 4-naphthaquinones with 2 : 3-dichloro-1 : 4-naphthaquinone,[8] of 2 : 5-diarylamino-*p*-benzoquinones with chloranil, and of 1-aryl-2 : 5-dimethylpyrroles by condensation with acetonylacetone.[9] 2-Amino-5-chloropyridine behaved like 2-aminopyridine towards ω-bromoacetophenones, readily undergoing

[1] Buu-Hoï, Gley, Xuong, and Bouffanais, *Compt. rend.*, 1954, **238**, 2582; Buu-Hoï, Gley, Bouffanais, Xuong, and Nam, *Experientia*, 1956, **12**, 73.
[2] Mayer, Eisman, and Konopka, *Proc. Soc. Exp. Biol.*, 1953, **82**, 498; Huebner, Marsh, Mizzoni, Mull, Schraeder, Troxell, and Scholz, *J. Amer. Chem. Soc.*, 1953, **75**, 2274.
[3] Buu-Hoï, *Internat. J. Leprosy*, 1954, **22**, 16; Buu-Hoï, Khuyen, and Xuong, *Bull. Acad. nat. Méd.*, 1955, **15/16**, 275; 1957, **9/10**, 1954.
[4] Cf. Buu-Hoï and Xuong, *Compt. rend.*, 1953, **237**, 498.
[5] Beaver, Roman, and Stoffel, *J. Amer. Chem. Soc.*, 1957, **79**, 1936.
[6] Buu-Hoï, Xuong, and Nam, *J.*, 1955, 1573.
[7] Hugershoff, *Ber.*, 1899, **32**, 2246.
[8] Cf. Buu-Hoï, *Bull. Soc. chim. France*, 1944, **11**, 578; Buu-Hoï, Royer, and Hubert-Habart, *Rec. Trav. chim.*, 1954, **73**, 188.
[9] Cf. Knorr, *Ber.*, 1885, **18**, 2254; Buu-Hoï, *J.*, 1949, 2882.

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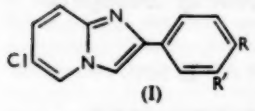
Tschitschibabin cyclisation[10] to give various 2-aryl-6-chloroiminazo[1,2-*a*]pyridines (I), which are of interest as potential antipurines. 4-Bromo-3-chloroaniline and 4-bromo-2-methylaniline were readily prepared from 3-chloroacetanilide and 2-methylacetanilide by means of *N*-bromosuccinimide[11] and subsequent hydrolysis; this method was also successfully applied to 3-fluoroacetanilide for the synthesis of 4-bromo-3-fluoroaniline. *N*-Chlorosuccinimide was used in a similar way for preparing 4-chloro-2-methylaniline from 2-methylacetanilide.



(I)

Tests *in vitro* against *Micrococcus pyogenes* var. *aureus* showed several polyhalogenated carbanilides and thiocarbanilides to be active in a concentration range $1 : 10^{-5}$—10^{-6}; notable activity *in vitro* and *in vivo* against *Mycobacterium tuberculosis* var. *hominis* (strain H37 Rv), as well as *in vivo* against *Mycobacterium leprae*, was shown by 4-diethylamino-4'-*iso*pentyloxythiocarbanilide.

Experimental

Preparation of 4-Bromo-3-chloroaniline.—A suspension of 3-chloroacetanilide (34 g.) and *N*-bromosuccinimide (36 g.) in dry carbon tetrachloride (300 c.c.) was refluxed for 4 hr.; after cooling, the solid precipitate was filtered off and treated with hot water to dissolve the succinimide, and the remaining 4-bromo-3-chloroacetanilide was heated with hydrochloric acid (50 c.c.) in 70% aqueous ethanol (100 c.c.) for 1 hr. After cooling and basification with ammonia, 4-bromo-3-chloroaniline (38 g.), m. p. 68° (from aqueous ethanol), was obtained. This procedure gave an amine free from isomers and by-products. 4-Bromo-2-methylaniline (36 g.), m. p. 55°, was similarly prepared from 2-methylacetanilide (30 g.) and *N*-bromosuccinimide (36 g.) in carbon tetrachloride.

4-Bromo-3-fluoroaniline.—3-Fluoroacetanilide (30 g.) and *N*-bromosuccinimide (36 g.) in carbon tetrachloride (250 c.c.) were treated as above, giving *4-bromo-3-fluoroacetanilide* (40 g.),

Substituted carbanilides.

	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
2 : 4-Difluoro	222°	$C_{13}H_{10}ON_2F_2$	62·8	4·1	62·9	4·0
3 : 4-Difluoro	216	$C_{13}H_{10}ON_2F_2$	62·9	4·1	62·9	4·0
4-Chloro-2' : 4'-difluoro	262	$C_{13}H_9ON_2ClF_2$	55·1	3·1	55·2	3·2
4-Chloro-3' : 4'-difluoro	246	$C_{13}H_9ON_2ClF_2$	55·0	3·1	55·2	3·2
4-Bromo-3-fluoro	230	$C_{13}H_{10}ON_2BrF$	50·3	3·3	50·5	3·3
4-Bromo-3' : 5'-dichloro-3-fluoro	257	$C_{13}H_8ON_2Cl_2BrF$	41·0	2·0	41·3	2·1
4-Bromo-4'-chloro-3-fluoro	289	$C_{13}H_9ON_2ClBrF$	45·6	2·7	45·5	2·7
3 : 5 : 3'-Trichloro	233	$C_{13}H_9ON_2Cl_3$	49·3	3·2	49·5	2·9
3 : 5 : 3' : 4'-Tetrachloro	265	$C_{13}H_8ON_2Cl_4$	44·3	2·6	44·6	2·3
3 : 5 : 2' : 3'-Tetrachloro	272	$C_{13}H_8ON_2Cl_4$	44·3	2·5	44·6	2·3
4-Bromo-3 : 3' : 5'-trichloro	273	$C_{13}H_8ON_2Cl_3Br$	39·5	2·0	39·6	2·0
3 : 5-Dichloro-2' : 4'-difluoro	229	$C_{13}H_8ON_2Cl_2F_2$	49·2	2·5	49·3	2·5
3 : 5-Dichloro-3' : 4'-difluoro	232	$C_{13}H_8ON_2Cl_2F_2$	49·0	2·6	49·3	2·5
2-Trifluoromethyl	182	$C_{14}H_{11}ON_2F_3$	60·3	4·0	60·1	4·0
4-Acetyl	186	$C_{15}H_{14}O_2N_2$	71·0	5·5	70·9	5·6
4-Acetyl-4'-fluoro	218	$C_{15}H_{13}O_2N_2F$	66·0	5·0	66·2	4·8
4-Acetyl-4'-chloro	233	$C_{15}H_{13}O_2N_2Cl$	62·1	4·3	62·4	4·5
4-Acetyl-3' : 5'-dichloro	236	$C_{15}H_{12}O_2N_2Cl_2$	55·8	3·8	55·8	3·7
4-Acetyl-3' : 4'-dichloro	259	$C_{15}H_{12}O_2N_2Cl_2$	55·6	3·8	55·8	3·7
4-Benzoyl	203	$C_{20}H_{16}O_2N_2$	75·8	5·4	75·9	5·1
4-Benzoyl-4'-chloro	250	$C_{20}H_{15}O_2N_2Cl$	68·3	4·2	68·5	4·3
4-*NN*-Diethylamino	189	$C_{17}H_{21}ON_3$	72·0	7·6	72·1	7·5
4'-Diethylamino-4-fluoro	213	$C_{17}H_{20}ON_3F$	67·5	6·6	67·8	6·7
4-Chloro-4'-diethylamino	227	$C_{17}H_{20}ON_3Cl$	64·2	6·3	64·3	6·4
2 : 4-Dichloro-4'-diethylamino	177	$C_{17}H_{19}ON_3Cl_2$	57·7	5·5	58·0	5·4
3 : 5-Dichloro-4'-diethylamino	180	$C_{17}H_{19}ON_3Cl_2$	58·2	5·4	58·0	5·4
4-*NN*-Dipropylamino	155	$C_{19}H_{25}ON_3$	73·5	8·2	73·4	8·1
4-Fluoro-4'-*NN*-dipropylamino	144	$C_{19}H_{24}ON_3F$	69·6	7·6	69·4	7·4
4-Chloro-4'-*NN*-dipropylamino	169	$C_{19}H_{24}ON_3Cl$	65·7	7·2	66·0	6·9

[10] Tschitschibabin *et al.*, *Ber.*, 1925, **58**, 1704; 1926, **59**, 2048; 1931, **64**, 2842; Buu-Hoï, Jacquignon, Xuong, and Lavit, *J. Org. Chem.*, 1954, **19**, 1370.
[11] Buu-Hoï, *Rev. Trav. chim.*, 1954, **73**, 197.

Ureas derived from nitrogen heterocycles.

	M. p.	Formula	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H
(a) N-(5-*Chloro*-2-*pyridyl*)*ureas.*						
N'-Phenyl	214°	$C_{12}H_{10}ON_3Cl$	57·9	4·0	58·2	4·1
N'-*p*-Chlorophenyl	236	$C_{12}H_9ON_3Cl_2$	51·0	3·3	51·1	3·2
N'-*p*-Fluorophenyl	216	$C_{12}H_9ON_3FCl$	54·0	3·2	54·3	3·4
N'-(3 : 4-Dichlorophenyl)	277	$C_{12}H_8ON_3Cl_3$	45·5	2·8	45·5	2·6
N'-(3 : 5-Dichlorophenyl)	284	$C_{12}H_8ON_3Cl_3$	45·5	2·7	45·5	2·6
(b) N-(5-*Nitro*-2-*pyridyl*)*ureas.*						
N'-Phenyl	238	$C_{12}H_{10}O_3N_4$	56·0	4·2	55·9	3·9
N'-*p*-Chlorophenyl	285	$C_{12}H_9O_3N_4Cl$	49·0	3·0	49·3	3·1
N'-*p*-Fluorophenyl	283	$C_{12}H_9O_3N_4F$	52·0	3·5	52·2	3·3
N'-(3 : 4-Dichlorophenyl)	291	$C_{12}H_8O_3N_4Cl_2$	44·0	2·5	44·1	2·5
N'-(3 : 5-Dichlorophenyl)	268	$C_{12}H_8O_3N_4Cl_2$	43·8	2·7	44·1	2·5
(c) N-(5-*Nitro*-2-*thiazolyl*)*ureas*						
N'-Phenyl	259	$C_{10}H_8O_3N_4S$	45·2	3·0	45·5	3·1
N'-*p*-Chlorophenyl	284	$C_{10}H_7O_3N_4ClS$	40·0	2·6	40·2	2·4
N'-*p*-Fluorophenyl	254	$C_{10}H_7O_3N_4FS$	42·5	2·5	42·6	2·5
N'-(3 : 4-Dichlorophenyl)	296	$C_{10}H_6O_3N_4Cl_2S$	35·8	1·9	36·1	1·8
(d) N-2-*Pyrimidylureas.*						
N'-*p*-Chlorophenyl	238	$C_{11}H_9ON_4Cl$	53·0	3·9	53·2	3·7
N'-*p*-Fluorophenyl	234	$C_{11}H_9ON_4F$	56·6	4·0	56·9	3·9
N'-(3 : 4-Dichlorophenyl)	253	$C_{11}H_8ON_4Cl_2$	46·4	3·0	46·7	2·8
N'-(3 : 5-Dichlorophenyl)	275	$C_{11}H_8ON_4Cl_2$	46·5	2·8	46·7	2·8
(e) N-(4 : 6-*Dimethyl*-2-*pyrimidyl*)*ureas.*						
N'-*p*-Fluorophenyl	212	$C_{13}H_{13}ON_4F$	59·8	4·9	60·1	5·0
N'-*p*-Chlorophenyl	216	$C_{13}H_{13}ON_4Cl$	56·3	4·9	56·5	4·7
N'-(3 : 4-Dichlorophenyl)	232	$C_{13}H_{12}ON_4Cl_2$	50·1	3·9	50·2	3·9
N'-(3 : 5-Dichlorophenyl)	236	$C_{13}H_{12}ON_4Cl_2$	50·0	4·1	50·2	3·9
(f) N-(2 : 4-*Dimethyl*-6-*pyrimidyl*)*ureas.*						
N'-*p*-Chlorophenyl	249	$C_{13}H_{13}ON_4Cl$	56·2	4·5	56·5	4·7
N'-(3 : 4-Dichlorophenyl)	251	$C_{13}H_{12}ON_4Cl_2$	50·0	4·0	50·2	3·9
N'-(3 : 5-Dichlorophenyl)	267	$C_{13}H_{12}ON_4Cl_2$	49·9	4·0	50·2	3·9

N-*Aryl*-N'-*pyridylthioureas.*

	M. p.	Formula	Found N (%)	Reqd. N (%)
N-*p*-Fluorophenyl-*N'*-3-pyridyl	190°	$C_{12}H_{10}N_3FS$	16·9	17·0
N-*p*-Chlorophenyl-*N'*-3-pyridyl	198	$C_{12}H_{10}N_3ClS$	15·6	15·9
N-*p*-Bromophenyl-*N'*-3-pyridyl	220	$C_{12}H_{10}N_3BrS$	13·6	13·6
N-*p*-Tolyl-*N'*-3-pyridyl	175	$C_{13}H_{13}N_3S$	17·2	17·3
N-(2 : 4-Xylyl)-*N'*-3-pyridyl	172	$C_{14}H_{15}N_3S$	16·0	16·3
N-*p*-Methoxyphenyl-*N'*-3-pyridyl	201	$C_{13}H_{13}ON_3S$	16·0	16·2
N-*p*-Ethoxyphenyl-*N'*-3-pyridyl	178	$C_{14}H_{15}ON_3S$	15·3	15·4
N-*p*-*iso*Pentyloxyphenyl-*N'*-3-pyridyl	136	$C_{17}H_{21}ON_3S$	13·3	13·3
N-*p*-Fluorophenyl-*N'*-(4-methyl-2-pyridyl)	182	$C_{13}H_{12}N_3FS$	16·0	16·1
N-*p*-Chlorophenyl-*N'*-(4-methyl-2-pyridyl)	216	$C_{13}H_{12}N_3ClS$	14·9	15·1
N-*p*-Bromophenyl-*N'*-(4-methyl-2-pyridyl)	222	$C_{13}H_{12}N_3BrS$	12·9	13·0
N-*p*-Fluorophenyl-*N'*-(5-methyl-2-pyridyl)	202	$C_{13}H_{12}N_3FS$	15·8	16·1
N-*p*-Chlorophenyl-*N'*-(5-methyl-2-pyridyl)	212	$C_{13}H_{12}N_3ClS$	15·0	15·1
N-*p*-Bromophenyl-*N'*-(5-methyl-2-pyridyl)	219	$C_{13}H_{12}N_3BrS$	12·9	13·0
N-*p*-Tolyl-*N'*-(5-methyl-2-pyridyl)	182	$C_{14}H_{15}N_3S$	16·5	16·3
N-(2 : 4-Xylyl)-*N'*-(5-methyl-2-pyridyl)	200	$C_{15}H_{17}N_3S$	15·2	15·5
N-*p*-Methoxyphenyl-*N'*-(5-methyl-2-pyridyl)	214	$C_{14}H_{15}ON_3S$	15·2	15·4
N-*p*-Ethoxyphenyl-*N'*-(5-methyl-2-pyridyl)	190	$C_{15}H_{17}ON_3S$	14·5	14·6
N-*p*-*iso*Pentyloxyphenyl-*N'*-(5-methyl-2-pyridyl)	132	$C_{18}H_{23}ON_3S$	12·8	12·8
N-*p*-Fluorophenyl-*N'*-(5-chloro-2-pyridyl)	198	$C_{12}H_9N_3ClFS$	14·6	14·9
N-*p*-Chlorophenyl-*N'*-(5-chloro-2-pyridyl)	230	$C_{12}H_9N_3Cl_2S$	14·0	14·1
N-*p*-Bromophenyl-*N'*-(5-chloro-2-pyridyl)	238	$C_{12}H_9N_3ClBrS$	12·0	12·3
N-Phenyl-*N'*-(5-chloro-2-pyridyl)	195	$C_{12}H_{10}N_3ClS$	16·0	15·9
N-*p*-Tolyl-*N'*-(5-chloro-2-pyridyl)	194	$C_{13}H_{12}N_3ClS$	14·9	15·1
N-*p*-Ethylphenyl-*N'*-(5-chloro-2-pyridyl)	173	$C_{14}H_{14}N_3ClS$	14·3	14·4
N-*p*-Methoxyphenyl-*N'*-(5-chloro-2-pyridyl)	226	$C_{13}H_{12}ON_3ClS$	14·0	14·3
N-*p*-Ethoxyphenyl-*N'*-(5-chloro-2-pyridyl)	181	$C_{14}H_{14}ON_3ClS$	13·6	13·7
N-*p*-*iso*Pentyloxyphenyl-*N'*-(5-chloro-2-pyridyl)	151	$C_{17}H_{23}ON_3ClS$	11·9	12·0

XUM

Thiocarbanilides.

	M. p.	Formula	Found N (%)	Reqd. N (%)
4-Bromo-3 : 4′-difluoro	185°	$C_{13}H_9N_2BrF_2S$	8·1	8·2
4 : 4′-Dibromo-3-fluoro	213	$C_{13}H_9N_2Br_2FS$	7·1	6·9
3 : 4-Dichloro-4′-fluoro	135	$C_{13}H_9N_2Cl_2FS$	8·6	8·9
3 : 5-Dichloro-4′-fluoro	176	$C_{13}H_9N_2Cl_2FS$	8·8	8·9
3 : 4 : 4′-Trichloro	160	$C_{13}H_9N_2Cl_3S$	8·2	8·4
4-Bromo-3′ : 4′-dichloro	172	$C_{13}H_9N_2Cl_2BrS$	7·3	7·4
2 : 3-Dichloro-4′-fluoro	161	$C_{13}H_9N_2Cl_2FS$	9·1	8·9
2 : 3 : 4′-Trichloro	199	$C_{13}H_9N_2Cl_3S$	8·1	8·4
4-Bromo-2′ : 3′-dichloro	201	$C_{13}H_9N_2Cl_2BrS$	7·6	7·4
2-Bromo-4′-fluoro	188	$C_{13}H_{10}N_2BrFS$	8·6	8·6
2-Bromo-4′-chloro	198	$C_{13}H_{10}N_2ClBrS$	8·0	8·2
2 : 4′-Dibromo	202	$C_{13}H_{10}N_2Br_2S$	7·0	7·3
2-Bromo-4′-methoxy	181	$C_{14}H_{13}ON_2BrS$	8·1	8·3
2-Bromo-4′-ethoxy	190	$C_{15}H_{15}ON_2BrS$	8·2	8·0
2-Bromo-4′-ethyl	185	$C_{15}H_{15}N_2BrS$	8·1	8·4
2-Bromo-4′-methyl	193	$C_{14}H_{13}N_2BrS$	8·8	8·7
2-Bromo-2′ : 4′-dimethyl	170	$C_{15}H_{15}N_2BrS$	8·5	8·4
3-Bromo-4′-fluoro	128	$C_{13}H_{10}N_2BrFS$	8·6	8·6
3-Bromo-4′-chloro	133	$C_{13}H_{10}N_2ClBrS$	8·4	8·2
3 : 4′-Dibromo	162	$C_{13}H_{10}N_2Br_2S$	7·0	7·3
3-Bromo-4′-methyl	135	$C_{14}H_{13}N_2BrS$	8·5	8·7
3-Bromo-2′ : 4′-dimethyl	133	$C_{15}H_{15}N_2BrS$	8·2	8·4
3-Bromo-4′-ethoxy	129	$C_{15}H_{15}ON_2BrS$	7·8	8·0
3-Bromo-4′-*iso*pentyloxy	119	$C_{18}H_{21}ON_2BrS$	7·0	7·1
4-Fluoro-4′-iodo	167	$C_{13}H_{10}N_2FIS$	7·2	7·5
4-Chloro-4′-iodo	213	$C_{13}H_{10}N_2ClIS$	7·2	7·2
4-Bromo-4′-iodo	224	$C_{13}H_{10}N_2BrIS$	6·6	6·5
4-Bromo-4′-ethoxy	197	$C_{15}H_{15}ON_2BrS$	8·1	8·0
4-Bromo-4′-*iso*pentyloxy	192	$C_{18}H_{21}ON_2BrS$	7·1	7·1
3 : 4-Difluoro	148	$C_{13}H_{10}N_2F_2S$	10·6	10·6
3 : 4 : 4′-Trifluoro	162	$C_{13}H_9N_2F_3S$	10·0	9·9
4-Chloro-3′ : 4′-difluoro	164	$C_{13}H_9N_2ClF_2S$	9·1	9·4
4-Bromo-3′ : 4′-difluoro	178	$C_{13}H_9N_2BrF_2S$	8·2	8·2
4-Ethyl-3′ : 4′-difluoro	136	$C_{15}H_{14}N_2F_2S$	9·5	9·6
3 : 4-Difluoro-2′ : 4′-dimethyl	151	$C_{15}H_{14}N_2F_2S$	9·5	9·6
4-Ethoxy-3′ : 4′-difluoro	163	$C_{15}H_{14}ON_2F_2S$	9·0	9·1
3 : 4-Difluoro-4′-*iso*pentyloxy	146	$C_{19}H_{20}ON_2F_2S$	7·8	8·0
2 : 4-Difluoro	136	$C_{13}H_{10}N_2F_2S$	10·3	10·6
2 : 4 : 4′-Trifluoro	176	$C_{13}H_9N_2F_3S$	9·7	9·9
4-Bromo-2′ : 4′-difluoro	190	$C_{13}H_9N_2BrF_2S$	8·0	8·2
4-Ethyl-2′ : 4′-difluoro	155	$C_{15}H_{14}N_2F_2S$	9·3	9·6
2 : 4-Difluoro-2′ : 4′-dimethyl	149	$C_{15}H_{14}N_2F_2S$	9·8	9·6
4-Ethoxy-2′ : 4′-difluoro	148	$C_{15}H_{14}ON_2F_2S$	9·0	9·1
2 : 4-Difluoro-4′-*iso*pentyloxy	132	$C_{19}H_{20}ON_2F_2S$	7·9	8·0
4-Bromo-3-chloro-4′-fluoro	178	$C_{13}H_9N_2ClBrFS$	7·5	7·8
4-Bromo-3′ : 4′-dichloro	187	$C_{13}H_9N_2Cl_2BrS$	7·5	7·4
4 : 4′-Dibromo-3-chloro	191	$C_{13}H_9N_2ClBr_2S$	6·4	6·7
4 : 4′-Dibromo-3 : 3′-dichloro [a]	216	$C_{13}H_8N_2Cl_2Br_2S$	6·0	6·2
4-Chloro-4′-fluoro-2-methyl	117	$C_{14}H_{12}N_2ClFS$	9·2	9·5
4 : 4′-Dichloro-2-methyl	150	$C_{14}H_{12}N_2Cl_2S$	8·8	9·0
4-Bromo-4′-chloro-2′-methyl	167	$C_{14}H_{12}N_2ClBrS$	7·6	7·9
4 : 4′-Dibromo-2-methyl	185	$C_{14}H_{12}N_2Br_2S$	6·9	7·0
4-Bromo-4′-chloro-2-methyl	172	$C_{14}H_{12}N_2ClBrS$	7·7	7·9
4-*NN*-Diethylamino-4′-fluoro	148	$C_{17}H_{20}N_3FS$	13·4	13·2
4-Chloro-4′-*NN*-diethylamino	173	$C_{17}H_{20}N_3ClS$	12·5	12·6
4-Bromo-4′-*NN*-diethylamino	199	$C_{17}H_{20}N_3BrS$	11·0	11·1
4-*NN*-Dipropylamino-4′-fluoro	141	$C_{19}H_{24}N_3FS$	12·0	12·2
4-*NN*-Dipropylamino-4′-chloro	167	$C_{19}H_{24}N_3ClS$	11·3	11·6
4-Bromo-4′-*NN*-dipropylamino	172	$C_{19}H_{24}N_3BrS$	10·1	10·3
4-Chloro-4′-*NN*-diethylamino-2′-methyl	190	$C_{18}H_{22}N_3ClS$	12·0	12·1
2-Ethyl-4′-fluoro	120	$C_{15}H_{15}N_2FS$	10·0	10·2
4-Chloro-2′-ethyl	139	$C_{15}H_{15}N_2ClS$	9·3	9·6
2 : 4′-Diethyl	125	$C_{17}H_{20}N_2S$	9·5	9·8
4-Ethoxy-2′-ethyl	160	$C_{17}H_{20}ON_2S$	9·2	9·3
4-Chloro-4′-*cyclo*hexyl	229	$C_{19}H_{21}N_2ClS$	8·0	8·2
4-*cyclo*Hexyl	185	$C_{19}H_{22}N_2S$	8·9	9·0
4-*cyclo*Hexyl-2′-methoxy	176	$C_{20}H_{24}ON_2S$	8·3	8·2
4-*cyclo*Hexyl-4′-methyl	176	$C_{20}H_{24}N_2S$	8·3	8·6
4-Ethyl-4′-*cyclo*hexyl	151	$C_{21}H_{26}N_2S$	8·5	8·3

Thiocarbanilides (contd.).

	M. p.	Formula	Found N (%)	Reqd. N (%)
4-Ethoxy-4′-*cyclo*hexyl	170°	$C_{21}H_{26}ON_2S$	7·8	7·9
4-*cyclo*Hexyl-4′-*iso*pentyloxy	155	$C_{24}H_{32}ON_2S$	7·0	7·1
4-Fluoro-4′-*cyclo*hexyl	163	$C_{19}H_{21}N_2FS$	8·2	8·5
4-Fluoro-3′ : 4′-dimethyl	164	$C_{15}H_{15}N_2FS$	10·0	10·2
4-Chloro-3′ : 4′-dimethyl	168	$C_{15}H_{15}N_2ClS$	9·5	9·6
4-Bromo-3′ : 4′-dimethyl	172	$C_{15}H_{15}N_2BrS$	8·3	8·4
3 : 4 : 4′-Trimethyl	108	$C_{16}H_{18}N_2S$	10·1	10·4
2 : 4 : 3′ : 4′-Tetramethyl	128	$C_{17}H_{20}N_2S$	10·1	9·9
4-Methoxy-3′ : 4′-dimethyl	120	$C_{16}H_{18}ON_2S$	9·9	9·8
3 : 4-Dimethyl-4′-*iso*pentyloxy	105	$C_{20}H_{26}ON_2S$	8·0	8·2
4-Fluoro-2′ : 5′-dimethyl	147	$C_{15}H_{15}N_2FS$	10·0	10·2
4-Chloro-2′ : 5′-dimethyl	160	$C_{15}H_{15}N_2ClS$	9·4	9·6
4-Bromo-2′ : 5′-dimethyl	178	$C_{15}H_{15}N_2BrS$	8·3	8·4
2 : 4 : 2′ : 5′-Tetramethyl	133	$C_{17}H_{20}N_2S$	9·6	9·9
4-Methoxy-2′ : 5′-dimethyl	126	$C_{16}H_{18}ON_2S$	9·6	9·8
4-Ethoxy-2′ : 5′-dimethyl	119	$C_{17}H_{20}ON_2S$	9·5	9·3
4-Fluoro-2′ : 4′ : 5′-trimethyl	156	$C_{16}H_{17}N_2FS$	9·4	9·7
4-Chloro-2′ : 4′ : 5′-trimethyl	175	$C_{16}H_{17}N_2ClS$	9·0	9·1
4-Ethyl-2′-methyl-5′-propyl	116	$C_{19}H_{24}N_2S$	8·9	9·0
4-Ethoxy-2′-methyl-5′-propyl	93	$C_{19}H_{24}ON_2S$	8·4	8·5
4-Methoxy-2′-methyl-5′-propyl	113	$C_{19}H_{22}ON_2S$	8·6	8·9
5-Butyl-2-ethyl-4-fluoro	95	$C_{19}H_{23}N_2FS$	8·1	8·4
5-Butyl-4′-ethoxy-2-ethyl	122	$C_{21}H_{28}ON_2S$	8·0	7·9
5-Butyl-2-ethyl-4′-methoxy	110	$C_{20}H_{26}ON_2S$	8·0	8·2
4-Acetamido	198	$C_{15}H_{15}ON_3S$	14·8	14·7
4-Acetamido-4′-methyl	224	$C_{16}H_{17}ON_3S$	14·2	14·0
4-Acetamido-2′ : 4′-dimethyl	184	$C_{17}H_{19}ON_3S$	13·1	13·4
4-Acetamido-4′-ethyl	199	$C_{17}H_{19}ON_3S$	13·2	13·4
4-Acetamido-4′-fluoro	220	$C_{15}H_{14}ON_3FS$	13·6	13·9
4-Acetamido-4′-bromo	229	$C_{15}H_{14}ON_3BrS$	11·4	11·5
4-Acetamido-4′-methoxy	216	$C_{16}H_{17}O_2N_3S$	13·5	13·3
4-Acetamido-4′-ethoxy	215	$C_{17}H_{19}O_2N_3S$	12·6	12·8
4-Acetamido-4′-*iso*pentyloxy	188	$C_{20}H_{25}O_2N_3S$	11·0	11·3
4 : 4′-Bis-(*NN*-diethylamino)	173	$C_{21}H_{30}N_4S$	15·0	15·1
4-*NN*-Diethylamino-4′-ethyl	147	$C_{19}H_{25}N_3S$	12·5	12·8
4-*NN*-Diethylamino-2′ : 4′-dimethyl	146	$C_{19}H_{25}N_3S$	12·6	12·8
4-*NN*-Diethylamino-4-ethoxy	153	$C_{19}H_{25}ON_3S$	12·1	12·2
4-*NN*-Diethylamino-4′-*iso*pentyloxy	132	$C_{22}H_{31}ON_3S$	10·6	10·9
4-*NN*-Dipropylamino-4′-ethyl	148	$C_{21}H_{29}N_3S$	11·8	11·8
4-*NN*-Diethylamino-2 : 4′-dimethyl	171	$C_{19}H_{25}N_3S$	13·1	12·9
4-*NN*-Diethylamino-2 : 3′-dimethyl	136	$C_{19}H_{25}N_3S$	13·0	12·9
4-*NN*-Diethylamino-4′-methoxy-2-methyl	165	$C_{19}H_{25}ON_3S$	12·1	12·3
4-*NN*-Diethylamino-2′-methoxy-2-methyl	151	$C_{19}H_{25}ON_3S$	12·0	12·3
4-*NN*-Diethylamino-2 : 2′ : 4′-trimethyl	168	$C_{20}H_{27}N_3S$	12·5	12·3

• Prepared from 4-bromo-3-chloroaniline (2 mol.), carbon disulphide (1 mol.), and sulphur in boiling ethanol; recrystallisation from ethanol–benzene.

forming needles, m. p. 152°, from methanol (Found: C, 41·4; H, 3·1. C_6H_7ONBrF requires C, 41·4; H, 3·0%). Deacetylation with hydrochloric acid yielded *4-bromo-3-fluoroaniline*, crystallising as leaflets, m. p. 72—73°, from water (Found: C, 37·6; H, 2·8. C_6H_5NBrF requires C, 37·9; H, 2·7%). This amine (2 mol.) was characterised by condensation with chloranil (1 mol.) in boiling ethanol, to give 3 : 6-*di*-(*4-bromo-3-fluoroanilino*)-2 : 5-*dichloro*-1 : 4-*benzoquinone*, brown-violet needles, m. p. >320°, from xylene (Found: C, 38·9; H, 1·7. $C_{18}H_8O_2N_2Cl_2Br_2F_2$ requires C, 39·1; H, 1·5%).

Chlorination of 2-Methylacetanilide.—A suspension of 2-methylacetanilide (45 g.) and *N*-chlorosuccinimide (35 g.) in carbon tetrachloride (300 c.c.) was refluxed for 4 hr., and the resulting 4-chloro-2-methylacetanilide was deacetylated in the usual way, giving 4-chloro-2-methylaniline (28 g.), b. p. 189—192°/40 mm., m. p. 30°.

Preparation of NN′-Disubstituted Ureas (see Table).—These compounds were obtained, mostly in almost theoretical yield, by adding a benzene solution of the aryl *iso*cyanate (1 mol.) to the amine (1 mol.) in an appropriate solvent (benzene, xylene, or anhydrous dioxan) at room temperature; the product was recrystallised from an anhydrous solvent. Sterically hindered amines reacted anomalously: with *o*-trifluoromethylaniline, phenyl *iso*cyanate gave

the expected unsymmetrical urea, but *p*-chlorophenyl *iso*cyanate gave 4 : 4'-dichlorocarbanilide, needles, m. p. 318°, from ethanol (Found: N, 9·9. Calc. for $C_{13}H_{10}ON_2Cl_2$: N, 10·0%). With the exception of ureas derived from 2-amino-5-nitrothiazole, which were yellow to orange-yellow, all the ureas were colourless.

N-*Phenyl*-N'-(5 : 6 : 7 : 8-*tetrahydro*-1-*naphthyl*)*urea* had m. p. 205° (Found: C, 76·8; H, 6·8. $C_{17}H_{18}ON_2$ requires C, 76·7; H, 6·8%), and the 4-*chloro*-5 : 6 : 7 : 8-*tetrahydro*-1-*naphthyl analogue* has m. p. 258° (Found: C, 67·8; H, 5·8. $C_{17}H_{17}ON_2Cl$ requires C, 68·0; H, 5·7%).

Preparation of NN'-*Disubstituted Thioureas.*—These were obtained, in lower yields than for the ureas, by treating the appropriate amine (1 mol.) in warm ethanol with the aryl *iso*thiocyanate (1 mol.); in most cases, the product solidified and recrystallised from ethanol, benzene, or toluene. Reaction was much slower and required slight heating at 60° when the amine and/or the *iso*thiocyanate was *ortho*-substituted. N-p-*Fluoro*-, m. p. 139° (Found: N, 9·1. $C_{17}H_{17}N_2FS$ requires N, 9·3%), N-p-*chloro*-, m. p. 192° (Found: N, 8·6. $C_{17}H_{17}N_2ClS$ requires LN, 7·8%), and N-p-*bromo-phenyl*-N'-(5 : 6 : 7 : 8-*tetrahydro*-1-*naphthyl*)*thiourea*, m. p. 196° (Found: N, 7·5. $C_{17}H_{17}N_2BrS$ requires N, 7·8%), were prepared.

Miscellaneous Unsymmetrical Ureas (*cf. Table*).—N-(1-*Acetyl*-7-*naphthyl*)-N'-p-*chlorophenyl-urea*, prepared from 7-amino-1-acetonaphthone,[12] formed needles, m. p. 242°, from benzene (Found: C, 67·3; H, 4·6. $C_{19}H_{15}O_2N_2Cl$ requires C, 67·4; H, 4·5%); N-p-*chlorophenyl*-N'-(2-*phenanthridinyl*)*urea*, obtained from 2-aminophenanthridine, formed needles, m. p. 280°, from benzene (Found: N, 11·8. $C_{20}H_{14}ON_3Cl$ requires N, 12·1%); N-(3 : 4-*dichlorophenyl*)-N'-6-*quinolylurea*, prepared from 6-aminoquinoline, crystallised as needles, m. p. 288°, from ethanol–benzene (Found: N, 12·5. $C_{16}H_{11}ON_3Cl_2$ requires N, 12·7%).

Substituted 2-*Chloro*-1 : 4-*naphthaquinones.*—These (see Table) were prepared by refluxing for 2 hr. an ethanolic solution of equimolar amounts of 2 : 3-dichloro-1 : 4-naphthaquinone and the appropriate arylamine in the presence of sodium acetate; the precipitate obtained on cooling was collected, washed with water, and recrystallised from ethanol or ethanol–benzene.

3-*Substituted* 2-*chloro*-1 : 4-*naphthaquinones.*

			Found (%)		Reqd. (%)	
3-Substituent [a]	M. p.	Formula	C	H	C	H
4-Bromo-3-chloroanilino	255°	$C_{16}H_8O_2NCl_2Br$	48·1	2·2	48·4	2·0
4-Chloro-2-methylanilino	213	$C_{17}H_{11}O_2NCl_2$	61·2	3·5	61·4	3·3
4-Bromo-2-methylanilino	218	$C_{17}H_{11}O_2NClBr$	54·2	2·6	54·2	2·9
3 : 5-Dichloroanilino	269	$C_{16}H_8O_2NCl_3$	54·3	2·3	54·5	2·3
2 : 4-Difluoroanilino	198	$C_{16}H_8O_2NClF_2$	60·0	2·7	60·1	2·5
3 : 4-Difluoroanilino	199	$C_{16}H_8O_2NClF_2$	59·8	2·7	60·1	2·5
p-*NN*-Diethylaminoanilino	159	$C_{20}H_{19}O_2N_2Cl$	68·0	5·7	67·8	5·4
p-*NN*-Dipropylaminoanilino	118	$C_{22}H_{23}O_2N_2Cl$	69·1	6·2	69·0	6·1

[a] Except for the last two compounds which were deep brown-violet, these quinones were deep red leaflets or prisms.

1-*Aryl*-2 : 5-*dimethylpyrroles.*—These compounds (see Table), synthesised for characterisation of some arylamines, were prepared by refluxing for a few hours the appropriate amine with acetonylacetone in slight excess, the product being distilled *in vacuo* and recrystallised from ligroin (b. p. 100—130°).

1-*Substituted* 2 : 5-*dimethylpyrroles.*

				Found (%)	Reqd. (%)
1-Substituent	B. p./mm.	M. p.	Formula	N	N
p-Diethylaminophenyl	181°/17	85°	$C_{16}H_{22}N_2$	11·5	11·6
p-Dipropylaminophenyl	208°/18	57	$C_{18}H_{26}N_2$	10·1	10·4
3 : 4-Difluorophenyl	155°/30	57	$C_{12}H_{11}NF_2$	7·0	6·8
4-Bromo-3-chlorophenyl	181°/18	58	$C_{12}H_{11}NBrCl$	5·0	4·9

6-*Chloro*-2-p-*chlorophenyliminazo*[1,2-a]*pyridine* (I; R = Cl, R' = H).—A solution of ω-bromo-4-chloroacetophenone (2·3 g.) and 2-amino-5-chloropyridine (1·3 g.) in ethanol (20 c.c.) was refluxed for 6 hr.; the precipitate obtained on cooling recrystallised from ethanol as needles (1·5 g.), m. p. 209° (Found: N, 10·9. $C_{13}H_8N_2Cl_2$ requires N, 10·6%). Similarly were prepared the 2-p-*bromophenyl*-6-*chloro*-, needles, m. p. 221° (from ethanol) (Found:

[12] Leonard and Hyson, *J. Amer. Chem. Soc.*, 1949, **71**, 1392.

N, 9·3. $C_{13}H_8N_2ClBr$ requires N, 9·1%), *6-chloro-2-p-fluorophenyl-*, m. p. 199° (from ethanol) (Found: N, 11·7. $C_{13}H_8N_2ClF$ requires N, 11·4%), and *2-(3-bromo-4-methoxyphenyl)-6-chloro-compound*, yellowish needles, m. p. 194° (from ethanol) (Found: N, 8·5. $C_{14}H_{10}ON_2ClBr$ requires N, 8·3%).

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574. *Glyoxalinopyrimidines. Part II.*[1]

By J. CLARK and G. R. RAMAGE.

Methyl and ethyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate (I; X = Cl, R = Me or Et) were condensed with 2-chloroethylamine, and the products (II; X = NO_2, R = Me or Et) were reduced and cyclised. It was established by unambiguous synthesis that the cyclisations yielded tetrahydroglyoxalino-pyrimidines (III; X = Cl, Y = CO_2Me or CO_2Et) and not the isomeric tetrahydropteridines (IV).

IT was shown by Ramage and Trappe [1] that 4-2′-chloroethylamino-5-nitropyrimidines, *e.g.*, (V; X = H), could be readily cyclised after the introduction into the 2-position of a group capable of initiating tautomerism (*e.g.*, OH, NH_2) or after reduction of the 5-nitro-group. Some 4-2′-chloroethylamino-5-nitropyrimidines with potentially tautomeric groups in both the 2- and the 6-position were also easily cyclised.[2] However, when certain 4-(*N*-benzyl-*N*-2-chloroethylamino)-5-nitro-compounds, *e.g.*, (V; X = CH_2Ph) were reduced, the products were 8-benzyltetrahydropteridines.[3]

The cyclisation of some 5-amino-4-2′-chloroethylaminopyrimidines with electron-demanding groups in both the 2- and the 4-position has now been studied. The compounds (II; X = NH_2, R = Me or Et) had a chlorine atom in the 2-position and a methoxycarbonyl or ethoxycarbonyl group in the 6-position. Both series were prepared because the methyl esters proved to have inconveniently low solubilities and indecisive melting points at certain stages.

5-Nitrouracil-4-carboxylic acid (I; X = OH, R = H) has been made by a number of authors [4] who simultaneously oxidised and nitrated 4-methyluracil but the reactions were violent, even on a small scale, and gave variable yields. The same compound has also been prepared by nitration of uracil-4-carboxylic acid with fuming nitric acid.[5] When the 4-methyluracil was nitrated and the resulting 4-methyl-5-nitrouracil oxidised as a separate stage the reactions proceeded smoothly and in good yield on the largest scale attempted.

The acid was esterified and converted into the dichloro-compounds (I; X = Cl, R = Me or Et) by standard methods. Selective replacement of one of the chlorine atoms in each of these compounds by a 2-chloroethylamino-group proved to be possible and in each case an excellent yield of a compound, assumed by analogy with other 2 : 4-dichloro-5-nitropyrimidines [2,6] to be 4-substituted, was obtained. The orientation of these substances was later confirmed by demonstrating an *o*-diamine arrangement in their reduction products (II; X = NH_2, R = Me or Et) which were converted into purines

[1] Part I, Ramage and Trappe, *J.*, 1952, 4410.
[2] Martin and Mathieu, *Tetrahedron*, 1957, **1**, 75.
[3] Brook and Ramage, *J.*, 1955, 896; *J.*, 1957, 1.
[4] Behrend and Roosen, *Annalen*, 1889, **251**, 238; Behrend, *ibid.*, 1885, **229**, 32; Köhler, *ibid.*, 1886, **236**, 34.
[5] Biltz and Kramer, *ibid.*, 1924, **436**, 165.
[6] Boon, Jones, and Ramage, *J.*, 1951, 96; Bitterli and Erlenmeyer, *Helv. Chim. Acta*, 1951, **34**, 835; Polonovski and Jérome, *Compt. rend.*, 1950, **230**, 392; Rose, *J.*, 1954, 4116; Brown, *J. Appl. Chem.*, 1957, **7**, 109.

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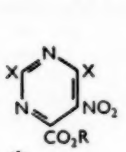
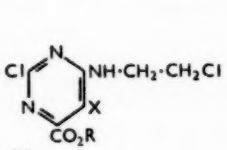
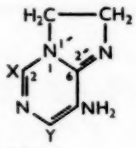
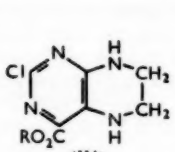
(VI; R = H, Me, or Et). The 5-amino-compounds themselves were fairly easily cyclised by heat in solution but it was possible to carry out the purine preparations using *NN*-dimethylformamide and phosphoryl chloride under very mild conditions, without interference from direct cyclisation.

Only moderate yields of amines were obtained by reducing the 5-nitro-compounds (II; X = NO_2, R = Me or Et) with Raney nickel and hydrogen. With these and certain other compounds in which an *o*-amino-ester arrangement was formed on reduction, the


(I)


(II)

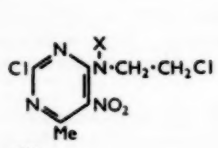

(III)

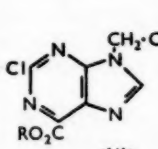

(IV)

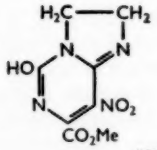
products appeared to interact with the catalyst. Better results were obtained by using powdered zinc and a little acetic or formic acid in methanol.

Methyl and ethyl 5-amino-4-2′-chloroethylaminopyrimidine-6-carboxylates (II; X = NH_2, R = Me or Et) were more stable to heat than similar compounds which did not contain two electron-demanding groups and much unchanged material was isolated from attempted cyclisations in boiling methanol as described for the preparation of a compound lacking the ester group (III; X = Cl, Y = H).[1] However, the compounds cyclised readily in boiling water and more slowly in boiling ethanol, yielding products which were shown to be tetrahydroglyoxalinopyrimidines (III; X = Cl, Y = CO_2Me or CO_2Et) and not the isomeric tetrahydropteridines.

The methyl and ethyl esters were shown to have cyclised in the same way by hydrolysing the cyclised products to the same carboxylic acid (III; X = Cl, Y = CO_2H) under conditions which did not affect the 2-chlorine atom.


(V)


(VI)


(VII)

The actual mode of cyclisation was then established by simultaneously hydrolysing the chlorine atom and the ester group of the compound (III; X = Cl, Y = CO_2Me) to obtain the hydroxy-carboxylic acid (III; X = OH, Y = CO_2H) which was then synthesised unambiguously. The alternative route involved hydrolysis and cyclisation of the pyrimidine (II; X = NO_2, R = Me). The product (VII), which could not have the pteridine ring system, was reduced by sodium dithionite to the corresponding amino-compound which yielded the required acid (III; X = OH, Y = CO_2H) on hydrolysis.

Experimental

M. p.s marked * were determined in a preheated bath, with rapid heating.

5-Nitrouracil-4-carboxylic Acid.—A mixture of 4-methyl-5-nitrouracil (40 g.) and nitric acid (100 c.c.; *d* 1·5) was heated for 4 hr. on the water-bath in a flask fitted with a short (50 cm.) air-condenser. The cooled mixture was filtered on sintered glass, and white solid which decomposed at 230° was washed successively with glacial acetic acid and ether. The yield (34—38 g.) was substantially reduced when a more efficient condenser or a less concentrated nitric acid was used.

Methyl 5-Nitrouracil-4-carboxylate.—5-Nitrouracil-4-carboxylic acid (50 g.), methanol (180 c.c.), and concentrated sulphuric acid (25 c.c.) were heated together, under reflux, for 8 hr. Next day the ester (44·5 g.) was filtered off, washed with methanol and, after drying, was suitable for use in the next stage. Crystallisation from water, followed by drying in air, gave a *monohydrate*, m. p. 199—200° (decomp.) (Found: C, 31·2; H, 3·0. $C_6H_5O_6N_3,H_2O$ requires C, 30·9; H, 3·0%). Anhydrous *methyl 5-nitrouracil-4-carboxylate* was obtained after drying at 65° *in vacuo* (Found: C, 33·7; H, 2·4; N, 19·7. $C_6H_5O_6N_3$ requires C, 33·5; H, 2·3; N, 19·5%).

Ethyl 5-nitrouracil-4-carboxylate (49 g.), m. p. 251° (decomp.), was similarly prepared from 5-nitrouracil-4-carboxylic acid (50 g.), ethanol (500 c.c.), and concentrated sulphuric acid (75 c.c.). Köhler [4] reports m. p. 250° (decomp.). The ethyl ester was much less soluble in ethanol than was the methyl ester in methanol.

Methyl 2 : 4-Dichloro-5-nitropyrimidine-6-carboxylate (I; X = Cl, R = Me).—A mixture of methyl 5-nitrouracil-4-carboxylate (15 g.), phosphoryl chloride (60 c.c.), and diethylaniline (20 c.c.) was set aside for 30 min. and then refluxed for 20 min. Excess of phosphoryl chloride was removed under reduced pressure and the cooled residue was poured on ice and extracted with ether. The ethereal solution was washed successively with N-hydrochloric acid, N-sodium hydrogen carbonate, and water, and then dried. After removal of the ether, the residue was distilled (13·8 g.; b. p. 140°/0·5 mm.); it rapidly solidified. *Methyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate* crystallised from *cyclo*hexane as prisms, m. p. 90—91° (Found: C, 29·0; H, 1·3; N, 16·5. $C_6H_3O_4N_3Cl_2$ requires C, 28·6; H, 1·2; N, 16·7%).

Ethyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate was similarly prepared from the corresponding ethyl ester but the period of reflux was advantageously extended to 1 hr. The product (15·2 g.; b. p. 128°/0·7 mm.) crystallised from *cyclo*hexane–light petroleum (b. p. 60—80°), yielding *ethyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate* as prisms, m. p. 37—38° (Found: C, 32·1; H, 1·8; Cl, 26·4. $C_7H_5O_4N_3Cl_2$ requires C, 31·6; H, 1·9; Cl, 26·7%). This compound was much more soluble in ether than was the corresponding methyl ester.

Methyl 2-Chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (II; X = NO_2, R = Me).—2-Chloroethylamine hydrochloride (6 g.) was added, with shaking, during 20 min. to a mixture of methyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate (12·6 g.) in chloroform (150 c.c.) and sodium hydrogen carbonate (12 g.) in water (40 c.c.). Shaking was continued for a further 20 min. after which the chloroform layer was separated, washed with water, and dried (Na_2SO_4). The chloroform was removed and crystallisation of the residue from methanol yielded *methyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate* (12·1 g.) as pale yellow prisms, m. p. 108° (Found: C, 32·7; H, 2·8. $C_8H_8O_4N_4Cl_2$ requires C, 32·6; H, 2·7%).

Ethyl 2 : 4-dichloro-5-nitropyrimidine-6-carboxylate (13·3 g.) was similarly condensed with 2-chloroethylamine hydrochloride (6 g.) and gave *ethyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate* (13·2 g.) which crystallised as pale yellow plates or needles, m. p. 92°, from methanol or *cyclo*hexane respectively (Found: C, 35·1; H, 3·3; N, 17·8. $C_9H_{10}O_4N_4Cl_2$ requires C, 35·0; H, 3·3; N, 18·1%).

Methyl 5-Amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate (II; X = NH_2, R = Me).—(*a*) Methyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (1 g.) in methanol (200 c.c.) was shaken with Raney nickel (3 c.c. of settled suspension) and hydrogen until the uptake reached the theoretical value for reduction of the nitro-group (3 hr.). The catalyst was removed and the solution was evaporated below 45° under reduced pressure to 10 c.c. *Methyl 5-amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate* (0·5 g., 55%) separated and crystallised from methanol as prisms which slowly decomposed above 140° (Found: C, 36·6; H, 3·9. $C_8H_{10}O_2N_4Cl_2$ requires C, 36·2; H, 3·8%).

Solutions of the amine exhibited a slight blue fluorescence in daylight and a strong blue fluorescence in ultraviolet light.

(*b*) Methyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (5 g.) in methanol (300 c.c.) was stirred vigorously and 90% formic acid (10 c.c.) was added, followed by powdered zinc (15 g.) in one addition. Stirring was continued for 5 min. and the warm mixture was then immediately filtered. The residue was washed with hot methanol (50 c.c.), and the pale yellow combined filtrates were evaporated as in (*a*) to about 15 c.c. To the partially crystallised mixture, cold water (150 c.c.) was added and the amine (3·9 g., 87%) was filtered off as well-formed white prisms identical with the product from (*a*). Further purification was unnecessary.

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Methyl 5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (III; X = Cl, Y = CO_2Me).—The total moist filtercake of crude material from the preceding experiment (*b*) was heated with water (60 c.c.), under reflux, for ¾ hr. The solution was cooled, made alkaline with dilute ammonia, and the *methyl 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate* (3·2 g.) which separated was filtered off. A sample crystallised from 2-ethoxyethanol as pale yellow prisms, m. p. 229° (decomp.) • (Found: C, 41·9; H, 4·0; Cl, 15·1. $C_8H_9O_3N_4Cl$ requires C, 42·0; H, 4·0; Cl, 15·5%). In solution the base exhibited a weak blue fluorescence in ultraviolet light.

The *picrate* crystallised from 2-ethoxyethanol as golden-yellow plates which slowly decomposed >230° [m. p. 246° (decomp.) •] (Found: C, 37·0; H, 2·8; Cl, 7·5. $C_8H_9O_2N_4Cl,C_6H_3O_7N_3$ requires C, 36·7; H, 2·6; Cl, 7·7%).

The stability was investigated by heating the amine (0·5 g.) in methanol (15 c.c.) under reflux for 2½ hr., the solvent being then evaporated under reduced pressure. The residue was treated with hot water (10 c.c.) to extract any cyclised hydrochloride and the water-insoluble part of the residue (0·17 g., 34%), which proved to be unchanged amine, was crystallised from methanol. The cyclised base (0·25 g., 58%), obtained by adding dilute ammonia to the solution of its hydrochloride, was identical with that prepared by cyclisation in water (above).

Ethyl 5-Amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate (II; X = NH_2, R = Et).—(*a*) Ethyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (1 g.) in ethanol (70 c.c.) was reduced with Raney nickel (1·5 c.c. of settled suspension) and hydrogen as described for the corresponding methyl ester (see above). *Ethyl 5-amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate* (0·55 g.) was obtained as prisms which partly melted, with decomposition, at 141° (Found: C, 38·9; H, 4·3; Cl, 25·5. $C_9H_{12}O_2N_4Cl_2$ requires C, 38·7; H, 4·3; Cl, 25·4%).

Solution of the substance exhibited a slight blue fluorescence in daylight and a strong blue fluorescence in ultraviolet light.

An acetyl compound was prepared by treatment with acetic anhydride at 80° for 1 hr. Excess of reagent was removed and the residue, treated with dilute ammonia, crystallised from benzene–*cyclo*hexane as needles, and dried in *vacuo* at 20°. In benzene solution, the *monoacetyl derivative*, m. p. 113—114°, exhibited an intense blue fluorescence in ultraviolet light (Found: C, 39·9, 39·7; H, 4·6, 4·6. $C_{11}H_{14}O_3N_4Cl_2,\frac{1}{2}H_2O$ requires C, 40·0; H, 4·6%).

(*b*) A solution of ethyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (2 g.) in methanol (75 c.c.) was reduced with glacial acetic acid (7·5 c.c.) and powdered zinc (5 g.) as described for the reduction, by zinc and formic acid, of the corresponding methyl ester. The amine (1·45 g., 80%) was obtained as colourless prisms, identical with those from the reduction (*a*). Pure starting material was necessary for the reduction by zinc and acetic acid and if 90% formic acid was substituted a lower yield of an impure, yellow product was obtained.

Ethyl 5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (III; X = Cl, Y = CO_2Et).—(*a*) Ethyl 5-amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate (1 g.) was heated with water (10 c.c.), under reflux, for 45 min. The resulting solution was cooled, treated with excess of dilute ammonia, and kept for 3 hr., then *ethyl 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate* (0·9 g.) was filtered off. It crystallised from aqueous 2-ethoxyethanol as very pale yellow prisms which, after drying *in vacuo* for 1 hr. at 60°, were still hydrated and melted at 153—154° (Found: C, 43·2, 43·4; H, 4·8, 5·0. $C_9H_{11}O_2N_4Cl,\frac{1}{2}H_2O$ requires C, 42·9; H, 4·8%). Solutions of the base showed a weak blue fluorescence in ultraviolet light.

Other hydrates were obtained by crystallisation from water: an aqueous solution kept at 20° deposited almost colourless prismatic needles which, after air drying for 24 hr., melted when rapidly heated to 110° (Found: C, 38·9; H, 5·5. $C_9H_{11}O_2N_4Cl,2H_2O$ requires C, 38·8; H, 5·4%). A more concentrated aqueous solution, kept at 55°, deposited chunky prisms which melted when rapidly heated to 140° (Found: C, 42·2; H, 5·0. $C_9H_{11}O_2N_4Cl,H_2O$ requires C, 41·5; H, 5·0%). When slowly heated both hydrates melted at 153—154°.

The anhydrous base, m. p. 153—154°, was obtained by drying a hydrate *in vacuo* at 130° for 3 hr. (Found: C, 44·5; H, 4·3. $C_9H_{11}O_2N_4Cl$ requires C, 44·5; H, 4·6%).

The *picrate* crystallised from 2-ethoxyethanol as bright yellow needles, m. p. 242° (decomp.) (Found: C, 38·4; H, 3·1. $C_9H_{11}O_2N_4Cl,C_6H_3O_7N_3$ requires C, 38·2; H, 3·0%).

(*b*) Ethyl 5-amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate (0·25 g.) was heated, under reflux, with ethanol (10 c.c.) for 2½ hr. The hydrochloride (0·25 g.) was filtered

off from the cooled solution, dissolved in warm water, and treated with excess of dilute ammonia. A base (0·18 g.), m. p. 154°, identical with that obtained by cyclisation in water, gradually crystallised.

5-Amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylic Acid (III; X = Cl, Y = CO_2H).—Hot 2N-sodium hydroxide (15 c.c.) was well stirred during the addition of a hot solution of methyl (or ethyl) 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (1 g.) in dioxan (30 c.c.) and for a further 3 min. The mixture was cooled and the precipitated *sodium 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate* was filtered off. A sample crystallised from water as needles which gradually decomposed above 250° and was analysed after drying at 100°/0·5 mm. for 2 hr. (Found: C, 28·8; H, 4·6; N, 19·3. $C_7H_6O_2N_4ClNa,3H_2O$ requires C, 28·9; H, 4·2; N, 19·3%).

The free *acid* (0·77 g.), obtained by treating a hot aqueous solution of the sodium salt with excess of acetic acid, was very sparingly soluble in ethanol, water, 2-ethoxyethanol, dimethylformamide, or nitrobenzene. A pure sample was prepared by filtering a hot dilute solution of the pure sodium salt into hot dilute hydrochloric acid. The product slowly separated as very pale yellow plates which did not melt below 250°. The crystals were boiled with water, filtered off, washed with ethanol, and dried at 100°/0·1 mm. for 2 hr. (Found: C, 39·0; H, 3·5. $C_7H_7O_2N_4Cl$ requires C, 39·2; H, 3·3%).

The *picrate*, which was prepared by treating a warm aqueous solution of the sodium salt with an excess of picric acid in ethanol, crystallised from water as yellow needles, m. p. 244° (decomp.) * (Found: C, 36·8; H, 2·8; Cl, 10·5. $C_7H_7O_2N_4Cl,\frac{1}{2}C_6H_3O_7N_3$ requires C, 36·5; H, 2·6; Cl, 10·8%).

5-Amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxyglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylic Acid (III; X = OH, Y = CO_2H).—Methyl (or ethyl) 5-amino-2-chloro-1 : 6 : 4′ : 5′-tetrahydroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (1 g.) was heated under reflux with 5N-hydrochloric acid (10 c.c.) for ½ hr. and the hydrochloride which separated on cooling was dissolved in boiling water (50 c.c.) and treated with a solution of sodium acetate trihydrate (3 g.) in water. After 24 hr., the product (0·5 g.) was filtered off and crystallised from water (charcoal). After several recrystallisations *5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxyglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylic acid* was obtained as yellow prisms which gradually decomposed above 240°; m. p. 268° (decomp.) * (Found: C, 43·1; H, 4·2; N, 28·8. $C_7H_8O_3N_4$ requires C, 42·9; H, 4·1; N, 28·6%).

A *picrate* was obtained as orange needles, m. p. 215° (decomp.) (Found: C, 38·9; H, 3·2; N, 24·9. $C_7H_8O_3N_4,\frac{1}{2}C_6H_3O_7N_3$ requires C, 38·7; H, 3·1; N, 24·8%). The *hydrochloride* crystallised from dilute hydrochloric acid as prismatic needles, decomp. >250° (Found: C, 34·0; H, 4·7; N, 21·9. $C_7H_8O_3N_4,HCl,H_2O$ requires C, 33·6; H, 4·4; N, 22·4%). The *mercury* salt of the *mercurichloride*, prepared by mixing hot, filtered aqueous solutions of the base and mercuric chloride, was very insoluble. It was prepared for analysis by extracting impurities with boiling *NN*-dimethylformamide and washing the residue with ethanol. The yellow needles, m. p. 236° (decomp.), were dried at 130°/1 mm. (Found: C, 19·8; H, 1·9; N, 12·6. $(C_7H_7O_3N_4)_2Hg,HgCl_2$ requires C, 19·5; H, 1·6; N, 13·0%).

(*b*) The same hydroxy-carboxylic acid (0·16 g.) was obtained when methyl 5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxyglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (0·2 g.) (see below) was boiled with 2N-sodium hydroxide (5 c.c.) for 2 min. and the mixture was treated with excess of acetic acid. The derivatives of this acid were identical with those previously obtained.

Methyl 1 : 6 : 4′ : 5′-Tetrahydro-2-hydroxy-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (VII).—Methyl 2-chloro-4-2′-chloroethylamino-5-nitropyrimidine-6-carboxylate (2·5 g.) was heated, under reflux, with glacial acetic acid (7·5 c.c.), water (7·5 c.c.) and sodium acetate trihydrate (2·5 g.) for 1½ hr. *Methyl 1 : 6 : 4′ : 5′-tetrahydro-2-hydroxy-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate* (1·7 g., 84%) separated from the cooled reaction mixture and crystallised from glacial acetic acid as prisms, m. p. 215° (decomp.) (Found: C, 40·3; H, 3·5. $C_8H_8O_5N_4$ requires C, 40·0; H, 3·4%).

Methyl 5-Amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxyglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (III; X = OH, Y = CO_2Me).—Methyl 1 : 6 : 4′ : 5′-tetrahydro-2-hydroxy-5-nitroglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate (1 g.) was stirred with N-sodium hydrogen carbonate (20 c.c.) during addition, in 6 min., of sodium dithionite (6 g.) and then for a further

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½ hr. The mixture was set aside for an hour, then filtered, and the *methyl 5-amino-1 : 6 : 4′ : 5′-tetrahydro-2-hydroxyglyoxalino(1′ : 2′-1 : 6)pyrimidine-4-carboxylate* (0·55 g.) was crystallised from water. It recrystallised from 2-ethoxyethanol as very pale yellow plates, m. p. 238° (decomp.)* (Found: C, 46·1; H, 4·7. $C_8H_{10}O_3N_4$ requires C, 45·7; H, 4·8%). The *picrate* crystallised from aqueous 2-ethoxyethanol as yellow prisms, m. p. 252—253° (decomp.)* (Found: C, 38·3; H, 3·1. $C_8H_{10}O_3N_4,C_6H_3O_7N_3$ requires C, 38·3; H, 3·0%).

Methyl and Ethyl 2-Chloro-9-2′-chloroethylpurine-6-carboxylate (VI; R = Me and Et).—A solution of methyl or ethyl 5-amino-2-chloro-4-2′-chloroethylaminopyrimidine-6-carboxylate (II; X = NH_2, R = Me or Et) (0·5 g.) in *NN*-dimethylformamide (10 c.c.) and phosphoryl chloride (1 c.c.) was kept for an hour before the volatile constituents were evaporated under reduced pressure on a boiling-water bath. The residue was treated with cold water (20 c.c.), and *methyl* or *ethyl 2-chloro-9-2′-chloroethylpurine-6-carboxylate* was filtered off and crystallised from ethanol as lustrous plates. The former (0·39 g.) had m. p. 189—190° (Found: C, 39·5; H, 3·0; N, 21·0. $C_9H_8O_2N_4Cl_2$ requires C, 39·3; H, 2·9; N, 20·4%), and the latter (0·28 g.), m. p. 128—129° (Found: C, 41·6; H, 3·6; N, 19·3. $C_{10}H_{10}O_2N_4Cl_2$ requires C, 41·5; H, 3·5; N, 19·4%).

The methyl ester purine was also prepared by carrying out the treatment with phosphoryl chloride and dimethylformamide on the water-bath for an hour. When these conditions were used with the ethyl ester, the product was contaminated with an impurity which raised the m. p. After 8 hr. on the water-bath enough of the impurity was produced to enable it to be isolated by repeated crystallisation from ethanol. It crystallised as plates, m. p. 180—183°, not depressed on admixture with methyl 2-chloro-9-2′-chloroethylpurine-6-carboxylate. The methyl ester raised the melting range of a pure sample of the ethyl ester, as did the impurity which was isolated. Conversion of an ethyl into a methyl ester had occurred under the more severe conditions.

2-Chloro-9-2′-chloroethylpurine-6-carboxylic Acid.—Methyl 2-chloro-9-2′-chloroethylpurine-6-carboxylate (0·4 g.) was heated, under reflux, with 2N-hydrochloric acid (8 c.c.) during 15 min. and the cooled mixture was filtered. The residue, dissolved in 2N-sodium hydrogen carbonate, was then heated with charcoal, filtered, and treated with excess of hydrochloric acid. *2-Chloro-9-2′-chloroethylpurine-6-carboxylic acid* (0·27 g.) separated as prisms, m. p. 206° (decomp.), and for analysis was reprecipitated twice more and extracted with a little hot water and then with boiling ethanol, then dried *in vacuo* at 80° (Found: C, 37·1; H, 2·4; N, 21·6. $C_8H_6O_2N_4Cl_2$ requires C, 36·8; H, 2·3; N, 21·5%). The material crystallised slowly and with considerable loss from water or 2-ethoxyethanol and was not affected by treatment with boiling concentrated hydrochloric acid during 30 min.

Solutions of the three purines described showed a weak blue fluorescence in ultraviolet light.

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575. α-1 : 4-*Glucosans. Part IX.* The Molecular Structure of a Starch-type Polysaccharide from* Dunaliella bioculata.

By B. P. Eddy, I. D. Fleming, and D. J. Manners.

A glucose-containing polysaccharide, isolated from the unicellular salt-water alga *Dunaliella bioculata*, has been examined by chemical and enzymic methods.

It resembles plant starches in many respects, but contains only 13% of amylose, and the amylopectin component has an average chain length of 15—16 glucose residues. Both components are incompletely degraded by β-amylase, the barriers to this enzyme being hydrolysed by Z-enzyme and isoamylase, respectively.

Although the polysaccharides isolated from red and brown seaweeds (Rhodophyceae and Phaeophyceae) have been extensively studied,[1,2] present knowledge of similar materials from green and blue-green algae (Chlorophyceae and Myxophyceae) is limited. The last two are, on the whole, less readily available. It is generally accepted [3] that the reserve carbohydrate of *Chlorella* is a starch, but precise structural details have not been reported. The green alga *Ulva expansa* contains an iodophilic polysaccharide which, unlike normal starches, shows no appreciable birefringence and gives an abnormal *X*-ray powder diagram.[4] Polysaccharides from *Oscillatoria* have been characterised as amylopectin [5] or glycogen [6] in type, and *Nitella* [5] contains a cellulose-type material. In contrast, *Nostoc* [5] yields a complex mucilage composed of uronic acids, rhamnose, xylose, galactose, and glucose, whilst green algae of the *Chlamydomonas* species synthesise soluble extracellular polysaccharides with galactose and arabinose as the main constituents.[7] This paper describes an examination of the storage polysaccharide from the halophytic unicellular alga *Dunaliella bioculata* (class, Chlorophyceae; order, Volvocales; family, Polyblepharidaceae). The food value of this organism has been reported elsewhere.[8]

A preliminary study of the dried algal cells showed the presence of glucosan which was extracted with water at 70° or 100°, or with potassium hydroxide solution (5% or 24%) at 20°. Since this material was stained blue-black with iodine, and was degraded by α-amylase, the presence of a starch-type polysaccharide was indicated. A sample of polysaccharide material extracted with hot water contained glucose (69%) and protein (23%). Attempts to separate these by extraction with chloral hydrate [9] or trichloroacetic acid and toluene were not successful. Although the protein content decreased to 6% and 3% respectively, some degradation of the polysaccharide (content 78 and 82% respectively) occurred. As an alternative method of extraction, the procedure of MacWilliam and his co-workers [10] was examined.

The dried cells were extracted with 30% aqueous perchloric acid at room temperature, and the resulting polysaccharide was then purified *via* the iodine complex. The product was amorphous, contained 99% of glucose and *ca.* 0·1% of protein, and an aqueous solution, which had $[\alpha]_D$ +169°, was stained blue with iodine, exhibiting maximum absorption at 600 mμ. On incubation with salivary α-amylase, an apparent percentage conversion into maltose (P_M) of 85 was observed; under similar conditions, potato starch had a P_M value

* Part VIII, Liddle and Manners, *J.*, 1957, 4708.

[1] Mori, *Adv. Carbohydrate Chem.*, 1953, **8**, 315.
[2] Black, *Ann. Reports*, 1953, **50**, 322.
[3] Fogg, "The Metabolism of Algae," Methuen and Co. Ltd., London, 1953.
[4] Meeuse and Kreger, *Biochim. Biophys. Acta*, 1954, **13**, 593.
[5] Hough, Jones, and Wadman, *J.*, 1952, 3393.
[6] Frederick, *Physiol. Plantarum*, 1951, **4**, 621.
[7] Lewin, *Canad. J. Microbiol.*, 1956, **2**, 665.
[8] Eddy, *J. Exp. Bot.*, 1956, **7**, 372.
[9] Meyer and Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 875.
[10] MacWilliam, Hall, and Harris, *J. Inst. Brewing*, 1956, **62**, 227.

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of 88. The polysaccharide was rapidly degraded by soya-bean β-amylase, giving 62% conversion into maltose; this degradation was increased to 83% by prior incubation with yeast isoamylase. The latter enzyme hydrolyses α-1 : 6-glucosidic inter-chain linkages in amylopectin and glycogen.[11]

The polysaccharide was oxidised at room temperature with potassium metaperiodate;[12] the production of formic acid corresponded to an average chain length ($\overline{CL}$) of 18 glucose residues, and the absence of glucose in an acid hydrolysate of the periodate-oxidised polysaccharide indicated that 1 : 2- or 1 : 3-glucosidic linkages were absent.[13]

The presence of an amylose-type component was shown by potentiometric titration[14] of the iodine complex, and the iodine binding power, kindly determined by Mr. J. M. G. Cowie, indicated an amylose content of 12—14%. The $\overline{CL}$ value of the amylopectin component was therefore 15—16 glucose residues. The small amount of formic acid which is liberated from the end-groups of amylose can, to a first approximation, be neglected. The polysaccharide was fractionated by the thymol method,[15] in the absence of oxygen, and the resulting fractions treated with β-amylase. The amylose component, with pure β-amylase, had a β-amylolysis limit of 73%, and on addition of barley β-amylase (which contains Z-enzyme[16]) the limit increased to 93%. The amylopectin fraction had β-amylolysis limits of 60% before, and 76% after, pre-treatment with isoamylase. The polymeric chains are therefore mainly composed of α-1 : 4-glucosidic linkages, and the outermost inter-chain linkages in the amylopectin are of the α-1 : 6-type.

The above evidence shows that the polysaccharide isolated from *Dunaliella bioculata* resembles normal plant starches in many respects. The interaction with iodine, the degradation by α- and β-amylase, and the separation into two components by thymol are typical properties. It is of interest that the algal amylose, like that from the potato and the wrinkled pea,[16] contains a small number of anomalous linkages which are not attacked by β-amylase.

The amylose content of the algal starch is unusually low (plant starches normally contain 20—30% of amylose[17]) and is similar to that of the starch synthesised by the flagellated protozoan *Polytomella coeca*.[18] Further, the amylopectin component has a relatively high degree of branching ($\overline{CL}$ values of 20—25 are usual[19]), which is similar to that of the polysaccharide from *Oscillatoria princeps*.[6] Both these organisms show high Q-enzyme (*i.e.*, amylo-1 : 4 ⟶ 1 : 6-transglucosidase) activity, and the present study suggests that *D. bioculata*, which can be readily cultivated under laboratory conditions, may also be a convenient source of this enzyme.

Experimental

The analytical methods and enzyme preparations used have been described in Parts IV,[20] VI,[21] and VII[16] of this series.

Isolation of Polysaccharide.—The algal cells, grown in artificial double-strength sea-water, were harvested by centrifugation, dried, and stored *in vacuo* over P_2O_5. Before extraction, the dried cells were disintegrated in a ball-mill and sieved (200 mesh).

In a preliminary experiment, ethanol was added to a hot-water extract of the powdered cells, to give an impure polysaccharide material [Found: reducing sugar (as glucose), 69·4%; N, 3·7%, equiv. to 23% of protein]. A portion was extracted with aqueous 33% chloral hydrate to give sample I [Found: glucose (by paper chromatography and cuprimetric titration),

[11] Manners and Khin Maung, *Chem. and Ind.*, 1955, 950.
[12] Halsall, Hirst, and Jones, *J.*, 1947, 1399; Bell and Manners, *J.*, 1952, 3641.
[13] Hirst, Jones, and Roudier, *J.*, 1948, 1779; Bell and Manners, *J.*, 1954, 1891.
[14] Anderson and Greenwood, *J.*, 1955, 3016.
[15] Haworth, Peat, and Sagrott, *Nature*, 1946, **157**, 19.
[16] Cowie, Fleming, Greenwood, and Manners, *J.*, 1954, 4430.
[17] Deatherage, MacMasters, and Rist, *Cereal Chem.*, 1955, **13**, 31.
[18] Bourne, Stacey, and Wilkinson, *J.*, 1950, 2694.
[19] Bell, *Ann. Reports*, 1947, **44**, 223.
[20] Fleming, Hirst, and Manners, *J.*, 1956, 2831.
[21] Liddle and Manners, *J.*, 1957, 3432.

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77·7; N, 0·9%]. A second portion was largely freed from protein by shaking it with 10% aqueous trichloroacetic acid and toluene, to yield sample II (Found: glucose, 81·7; N, 0·46%). Analysis by periodate oxidation and potentiometric iodine titration indicated that both samples had been degraded during purification.

A pure sample of undegraded polysaccharide was finally prepared by purification of a perchloric acid extract of the dried cells.[10] The latter (5 g.) were extracted three times with water (80 ml.) and 72% perchloric acid (60 ml.) by shaking for 30 min. at room temperature. Cell debris was removed by centrifugation, and the crude polysaccharide was precipitated and washed with acetone. An aqueous solution was then dialysed for 48 hr. against running tap-water. The volume was adjusted to 100 ml. and, to this, 20% sodium chloride solution (25 ml.) and iodine solution (3% in 3% potassium iodide; 10 ml.) were added with stirring. After several hours, the polysaccharide–iodine complex was collected, washed with alcoholic sodium chloride (2% in 75% ethanol), and decomposed by treatment with alcoholic sodium hydroxide (25 ml. of 5N-aqueous solution in 125 ml. of ethanol). The polysaccharide was washed again with alcoholic sodium chloride, dissolved in water, dialysed for 48 hr., and precipitated with acetone. This gave sample III (1 g.) (Found: glucose, 99·5; N, 0·02%). Sample III was a white amorphous powder which dissolved in warm water. The aqueous solution had $[\alpha]_D$ +169° (*c* 0·54) and was stained blue with iodine, exhibiting maximum absorption at 600 mμ.

The iodine-binding power of sample III was determined by Mr. J. M. G. Cowie using the method of Anderson and Greenwood.[14] It gave a typical starch titration curve, and extrapolation indicated the presence of 12—14% of amylose.

Enzymic Degradation.—(a) *Salivary α-amylase.* Polysaccharide (27·8 mg.), 0·1M-citrate–phosphate buffer (pH 7·0; 5 ml.), sodium chloride (5 mg.), and freeze-dried salivary α-amylase [21] (15 mg.) in a total volume of 50 ml. were incubated at 35° for 48 hr. The P_M value was 85. In a control experiment, potato starch (31·4 mg.) gave a P_M value of 88.

(b) *Soya-bean β-amylase.* Sample III (15·1 mg.) was incubated with 0·2M-acetate buffer (pH 4·6; 3 ml.), containing soya-bean β-amylase solution (0·05 ml.; 1000 units), in a total volume of 25 ml. After 24 and 48 hr., the β-amylolysis limit was 62%.

(c) *Isoamylase and β-amylase.* Sample III (29·1 mg.) in acetate buffer (pH 5·9; 5 ml.) and water (8 ml.) was treated with isoamylase solution (80 mg. in 2 ml.) at room temperature for 24 hr. (The isoamylase was extracted from brewer's yeast by Miss Zeenat H. Gunja.) After inactivation of the isoamylase by heat, soya-bean β-amylase solution (0·05 ml.) and water (to 50 ml.) were added. The β-amylolysis limit, after 24 hours' incubation at 35°, was 83%.

Potassium Metaperiodate Oxidation.—Sample III (174·5 mg.), dissolved in 3% potassium chloride solution (50 ml.), was oxidised with 8% sodium metaperiodate solution (8 ml.) at room temperature. Portions (10 ml.) were analysed at intervals:

Time of oxidn. (hr.)	50	100	200	300
Total formic acid prodn. (mg.)	1·99	2·50	2·76	2·80
Apparent $\overline{CL}$ (glucose residues)	24·9	19·8	18·0	17·7

Since the starch contains 13% of amylose, the amylopectin component has a $\overline{CL}$ value of 15—16 glucose residues. The remaining solution of periodate-oxidised starch was treated with ethylene glycol (5 ml.), dialysed for 48 hr., and freeze-dried. After acid hydrolysis with 2N-sulphuric acid for 2 hr. the neutralised hydrolysate was examined by paper chromatography. Glucose could not be detected.

Fractionation of the Starch.—Polysaccharide (*ca.* 200 mg.) was dissolved in boiling water (150 ml.) in an atmosphere of nitrogen. The solution was allowed to cool to 70° and powdered thymol (100 mg.) added. The temperature was maintained at 70° for 30 min. with continuous stirring, then the solution was set aside at room temperature for 2 days. The thymol–amylose complex was collected and dissolved in water (30 ml.). The supernatant solution was treated with acetone, and the precipitated polysaccharide collected, washed with acetone and dried (yield, *ca.* 170 mg.). This material gave a solution which was stained with iodine, showing maximum absorption at 560 mμ.

Enzymic Degradation of Starch Components.—(a) *Amylose.* The above solution of amylose (0·62 mg./ml. determined by acid hydrolysis) was incubated with acetate buffer (pH 4·6; 5 ml.) and soya-bean β-amylase solution (0·1 ml.) in a 50 ml. digest. After 24 hr. the β-amylolysis limit was 73%. Barley β-amylase (which contains Z-enzyme; 1500 units; 15 mg.) was then added. After a further 24 hr. the β-amylolysis limit was 93%.

(b) ***Amylopectin.*** The above precipitate (48·1 mg.) was incubated at pH 4·6 with barley β-amylase (3000 units; 30 mg.) in a final volume of 50 ml. The β-amylolysis limit was 60%.

[With ZEENAT H. GUNJA] Amylopectin (30·1 mg.) was incubated with isoamylase (50 mg.) at pH 5·9 and 20° in a 15 ml. digest for 18 hr. The isoamylase was inactivated by heat, β-amylase solution (3 ml.) added, and the maltose content determined. After 24 hr., the β-amylolysis limit was 76%.

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LOW TEMPERATURE STATION FOR RESEARCH IN BIOCHEMISTRY AND BIOPHYSICS, UNIVERSITY OF CAMBRIDGE, AND DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH [B. P. E.].
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH
[I. D. F. AND D. J. M.].

[*Received, March 18th,* 1958.]

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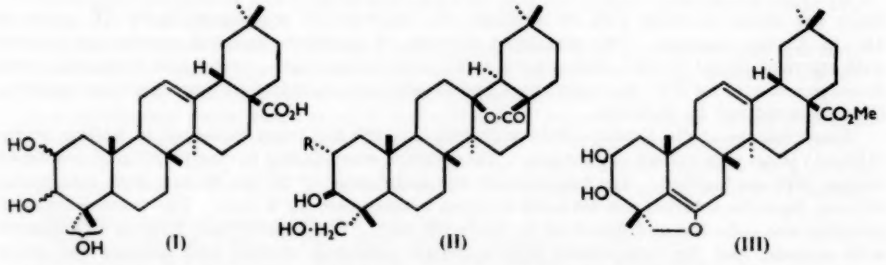
576. *The Stereochemistry of Arjunolic Acid.*

By F. E. KING, T. J. KING, and J. D. WHITE.

Arjunolic acid has been converted into 18α-hederagenin lactone, thereby demonstrating the conformation of the groups at positions 3 and 4. Stereospecific reduction, primarily of 2-oxo-18α-arjunolic lactone, indicate that the 2-hydroxyl substituent has the equatorial (α)-conformation; it follows that arjunolic acid is 2α : 3β : 23-trihydroxyolean-12-en-28-oic acid.

ARJUNOLIC ACID was discovered in *Terminalia arjuna* and its constitution shown [1] to be 2 : 3 : 23(or 24)-trihydroxyolean-12-en-28-oic acid (I). It has now been found in the wood, abura, of the West African tree, *Mitragyna ciliata*, from which it is conveniently isolated by ether-extraction.

When discussing the relative orientation of the secondary 2- and 3-hydroxyl groups of arjunolic acid it was suggested [1] that these substituents had the *trans*-equatorial (2α : 3β)-configuration, but no rigid support for this conclusion was then available, nor was there any evidence as to the conformation of the methyl and the hydroxymethyl groups at position 4. Experimental evidence has now been obtained which confirms our earlier opinions and establishes that the hydroxymethyl group has the equatorial (α-)conformation. The relevant observations are (i) the conversion of 18α-arjunolic lactone (II;



R = OH) into 18α-hederagenin lactone (II; R = H), the spatial arrangements at $C_{(3)}$ and $C_{(4)}$ then following from the well-known configuration of hederagenin,[2] and (ii) the results of stereospecific reduction of 2-oxoarjunolic lactone and the relative periodate oxidation rates of the two isomeric reduction products. Independent evidence bearing on

[1] King, King, and Ross, *J.*, 1954, 3995.
[2] Vogel, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1951, **34**, 2321.

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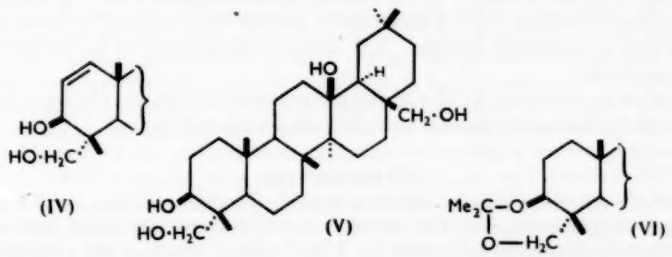
the conformation of the hydroxymethyl group was obtained in our work on terminolic acid (6β-hydroxyarjunolic acid),[3] since the formation from methyl terminonate of the anhydroterminonate formulated as (III), appeared to necessitate for the hydroxymethyl substituent an equatorial configuration. In conformity, Djerassi *et al.*[4] have shown, by a study of its rate of oxidation by lead tetra-acetate, that arjunolic acid is properly represented as a 2α : 3β-diol and quote structure (III) suggested for methyl anhydroterminonate as proof of the position of the third hydroxy-group at $C_{(23)}$.

Initial attempts to remove the 2-hydroxy-substituent in arjunolic lactone were unsuccessful: 2-oxoarjunolic lactone (II; R = O) was available through the previously unreported *iso*propylidenearjunolic lactone but was unstable to the conditions of the Huang-Minlon reduction and we were not able to convert it into a thioketal; pyrolysis of 2-benzoylarjunolic lactone (II; R = BzO) afforded a mixture which undoubtedly contained some of the olefin (IV) but catalytic reduction resulted mainly in hydrogenolysis, presumably of the 3-hydroxyl group in the allylic position. Success was achieved when 2-toluene-*p*-sulphonyl*iso*propylidenearjunolic lactone was reduced with lithium aluminium hydride. This reagent simultaneously reduced the lactone ring, and the product first isolated was a tetrol, presumably (V). Reconversion of this into the *iso*propylidene derivative for characterisation afforded a compound, the composition of which indicated partial loss of oxygen presumably by dehydration of the tertiary hydroxy-group. The structure of the tetrol and, in particular, the configuration of all four hydroxy-groups was established when hederagenin lactone diacetate gave an identical product on reduction with lithium aluminium hydride. Further proof of the configuration at positions 3 and 4 followed from the oxidation of the *iso*propylidene-diol (VI), obtained directly from the



*iso*propylidenetoluene-*p*-sulphonylarjunolic lactone, by permanganate to a lactone which was isolated as the diacetate and proved to be identical with hederagenin lactone diacetate.

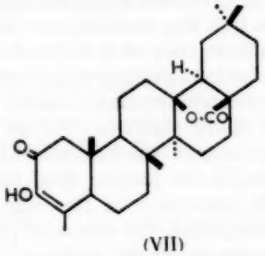
Before this direct proof of structure strong evidence for the 23-position of the primary hydroxy-group was gained from molecular-rotation considerations. The diosphenol (VII) obtained from arjunolic lactone [1] was reduced with sodium in alcohol to give, presumably, 2-hydroxyhedragenin lactone (VIII) whose molecular rotation was +128°. This corresponds to a change of +98° for the elimination of the CH_2·OH group from arjunolic lactone. This value agrees with the value of +103° for the rotation change in passing from methyl hederagenin to methyl hedragenin.

The β-equatorial orientation of the 3-hydroxy-group is further confirmed by the observation that diacetyl-3-oxoarjunolic lactone [1] is reduced by sodium borohydride to diacetylarjunolic lactone. It is well established that metal-hydride reduction of 3-oxo-groups in triterpenes gives predominantly the equatorial alcohol (the alkali-instability of the monoketone derived from arjunolic acid made it impossible to reduce by the more stereospecific sodium–alcohol). Further the absorption maximum shown by 2-oxo-arjunolic lactone (see above) at 270 mμ is at shorter wavelength than would be expected

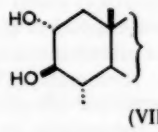
[3] King and King, *J.*, 1956, 4469.
[4] Djerassi, Thomas, Livingston, and Thompson, *J. Amer. Chem. Soc.*, 1957, **79**, 5292.

for a *cyclo*hexanone and it has been established [5] that the presence of a vicinal equatorial hydroxyl substituent shifts the absorption maximum of a carbonyl group by about 12 mμ to shorter wavelengths.

The stereochemistry at positions 3 and 4 having been established it remained only to fix the orientation at position 2. Here the evidence is not so direct but appears to be conclusive. Reduction of 2-oxoarjunolic lactone by sodium borohydride and by sodium in alcohol afforded different products which must be the pair of epimeric 2-alcohols. Sodium in alcohol produced arjunolic lactone: this method of reduction would be expected



(VII)



(VIII)

to give the thermodynamically more stable isomer and in the 2-position this should be the 2α-equatorial alcohol. Conversely metal-hydride reduction of sterically hindered ketones often gives the axial alcohol. 2-Oxoarjunolic lactone fails to give ketonic derivatives, so it is reasonable to assume that the borohydride reduction product (2-*epi*arjunolic lactone) consists of the 2β-axial isomer. In agreement, in semiquantitative experiments carried out in a spectrophotometer cell,[6] 2-*epi*arjunolic lactone was oxidised by periodate at least 10 times as fast as arjunolic lactone. The latter thus appears to be the *trans*- and the former the *cis*-isomer.

During other experiments 3 : 23 : 28-trihydroxyolean-12-ene was obtained by reduction of methyl *iso*propylidenehederagenin with lithium aluminium hydride.

Experimental

Except where otherwise stated, acylations were in pyridine and were carried out for 12—15 hr. at room temperature or for 1 hr. at 100°, and hydrolyses with alkali were under reflux with 2N-methanolic potassium hydroxide for 1 hr.; optical rotations are recorded for $CHCl_3$ solutions and sodium light at room temperature; and analytical samples were normally dried to constant weight at 150° in a vacuum or at 10° below the m. p. whichever was the lower.

O-iso*Propylidene*-18α-*arjunolic Lactone*.—18α-Arjunolic lactone (3 g.) was shaken in acetone (40 c.c.) containing 3 drops of concentrated hydrochloric acid until it was completely dissolved. Excess of anhydrous potassium carbonate was then added and after a further 20 min. the filtered solution was evaporated until crystals appeared. The iso*propylidene derivative* (2·7 g.) recrystallised from acetone as felted needles, m. p. 282—283°, containing acetone of crystallisation (Found: C, 73·7; H, 9·7. $C_{32}H_{52}O_5,C_3H_6O$ requires C, 73·7; H, 10·0. Found, after drying at 180°: C, 75·4; H, 10·1. $C_{32}H_{52}O_5$ requires C, 75·0; H, 9·9%). The *benzoate* separated as plates (from acetone), m. p. 309—310°, [α] +8·6° (*c* 1·05) (Found: C, 75·7; H, 8·9. $C_{40}H_{56}O_6$ requires C, 75·9; H, 8·9%).

Pyrolysis of the benzoate at 520—540°/0·5 mm. afforded a sublimate which still contained 10—15% of benzoate, as shown by its ultraviolet absorption spectrum. The sublimate did not absorb hydrogen over palladium catalysts and with Adams catalyst in the presence of perchloric acid an amorphous solid was obtained, analysis of which showed the partial loss of an oxygen atom.

18α-*Oleanane*-3 : 13 : 23 : 28-*tetrol*.—(*a*) The *iso*propylidenearjunolic lactone above was esterified with excess of toluene-*p*-sulphonyl chloride in pyridine (1 hr. at 100°). Working up in the usual way gave an amorphous solid containing sulphur. The crude sulphonate (1·1 g.)

[5] Cookson and Dandegaonker, *J.*, 1955, 352.
[6] Cf. Aspinall and Ferrier, *Chem. and Ind.*, 1957, 1216.

with lithium aluminium hydride (0·1 g.) was heated under reflux during 1 hr. in tetrahydrofuran (20 c.c.). The excess of hydride was decomposed with ethyl acetate, and the mixture poured into dilute hydrochloric acid and extracted with ether. After it had been washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$) the ether was evaporated, leaving a residue of the *tetrol* which crystallised from methanol containing a little hydrochloric acid as plates (0·55 g.), m. p. 275—280° raised by further crystallisation from methanol to 290—291°, [α] +34° (*c* 0·19 in pyridine) (Found: C, 75·6; H, 10·7. $C_{30}H_{52}O_4$ requires C, 75·6; H, 11·0%). Material which was obtained from a solution of the tetrol in acetone containing a little hydrochloric acid had m. p. 223—224° (Found: C, 77·5; H, 11·2. Calc. for $C_{33}H_{56}O_4$: C, 76·7; H, 10·9%).

(*b*) Hederagenin lactone diacetate (1·0 g.) was reduced by lithium aluminium hydride at 40° for 2 hr. in tetrahydrofuran. Working up as above gave 0·72 g. of plates, m. p. 292° (mixed m. p. with material from arjunolic lactone 290°), [α] +37° (*c* 0·5 in pyridine) (Found: C, 75·2; H, 11·2%). The infrared absorption curves of the products (*a*) and (*b*) were indistinguishable.

Hederagenin Lactone Diacetate.—The crude toluene-*p*-sulphonate described in (*a*) above was reduced as before and worked up by treatment with aqueous alkali instead of acid. The crude *iso*propylidene derivative obtained was dissolved in acetone containing potassium permanganate (0·1 g.). The mixture was kept at 40° for 5 min., then poured into aqueous sodium hydrogen sulphite and acidified. The precipitated solid was collected and warmed with dilute hydrochloric acid in methanol; the lactone which separated when the solution was cooled was acetylated, to give 0·04 g. of hederagenin lactone diacetate as plates (from methanol), m. p. and mixed m. p. 240—241°.

2-α-*Hydroxy*-18α-*hederagenin Lactone.*—To the diosphenol [1] (VII) (70 mg.) in ethanol (50 c.c.) was added, in small quantities, a total of 1 g. of sodium. The mixture was poured into water; the precipitated *lactone* crystallised from methanol as plates, m. p. 330° (decomp.), [α] +28° (*c* 0·11) (Found: C, 75·7; H, 9·9. $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%).

Reduction of Diacetyl-3-*oxo*-18α-*arjunolic Lactone.*—The ketone diacetate [1] (60 mg.) in dry methanol containing sodium hydrogen carbonate (100 mg.) was reduced overnight at room temperature with sodium borohydride (6 mg.). When the product was isolated in the usual way and acetylated, triacetyl-18α-arjunolic lactone, m. p. and mixed m. p. 263°, was obtained.

2-*Oxo*-18α-*arjunolic Lactone.*—*iso*Propylidenearjunolic lactone (1 g.) and potassium permanganate (75 mg.) were warmed in acetone at 40° for 30 min., then worked up in the usual way. Crystallisation of the product from methanol containing a trace of hydrochloric acid gave the *ketone* (0·9 g.) as needles, m. p. 340—344° (decomp.), [α] +22° (*c* 0·34 in EtOH) (Found: C, 73·9; H, 9·2. $C_{30}H_{46}O_5$ requires C, 74·0; H, 9·5%), $\lambda_{max.}$ 270 mμ (ε 40 in EtOH). The *diacetate*, purified by chromatography on acid-washed alumina, separated from methanol in needles, m. p. 292—293°, [α] +9° (*c* 0·1) (Found: C, 71·8; H, 9·2. $C_{34}H_{50}O_7$ requires C, 71·6; H, 8·8%).

The ketone failed to give an oxime, semicarbazone, or dinitrophenylhydrazone and did not react with ethane-thiol or -dithiol. After attempted Huang-Minlon reduction, only acidic material was recovered. The lactone ring in these compounds is stable to these conditions and the acidic products must have been formed by degradation of ring A.

Reduction of 2-*Oxo*-18α-*arjunolic Lactone.*—(*a*) Sodium (0·1 g.) was added to a solution of the ketone (0·1 g.) in dry ethanol. When the sodium had dissolved the mixture was poured into water, and the precipitated solid was crystallised from aqueous methanol, to give 18α-arjunolic lactone, m. p. 350—355° (decomp.) (triacetate, m. p. and mixed m. p. 263°).

(*b*) The ketone (75 mg.) was kept overnight at room temperature in dry methanol (25 c.c.) containing sodium borohydride (10 mg.), then the excess of borohydride was destroyed by dilute acid. The precipitated solid crystallised from methanol, giving 2-epi-18α-*arjunolic lactone* (55 mg.) as needles, m. p. 350—355° (Found: C, 73·7; H, 9·9. $C_{30}H_{48}O_5$ requires C, 73·7; H, 9·9%). The *triacetate* crystallised from methanol in needles, m. p. 268°, mixed m. p. with triacetylarjunolic lactone 235—242°, [α] ~0° (*c* 1·0) (Found: C, 70·3; H, 9·1. $C_{36}H_{54}O_8$ requires C, 70·3; H, 8·9%).

5 mg. of each of the above epimers were dissolved in 200 ml. of spectroscopic ethanol and mixed with 4 mg. of sodium periodate in 50 ml. of aqueous alcohol (1 : 1). The absorption of the resulting solutions at 223 mμ was observed. The solution containing arjunolic lactone showed a steady absorption value after 25 min. while that containing the epimer reached a steady state after only 2 min.

XUM

Olean-12-*ene*-3 : 23 : 28-*triol*.—Methyl *iso*propylidenehederagenin (0·2 g.) was reduced at room temperature in ether with lithium aluminium hydride (50 mg.). The mixture was worked up in the usual manner and the product was crystallised from methanol containing a little hydrochloric acid, to give the *triol* as needles, m. p. 250°, [α] +77° (*c* 0·42) (Found: C, 78·3; H, 11·0. $C_{30}H_{50}O_3$ requires C, 78·6; H, 11·0%).

Dibenzoyl-18α-*hederagenin Lactone*.—18α-Hederagenin lactone was benzoylated in the usual way, to give the *dibenzoate* as plates (from benzene), m. p. 314—315°, [α] +76° (*c* 0·48) (Found: C, 77·7; H, 8·6. $C_{44}H_{56}O_6$ requires C, 77·6; H, 8·3%).

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THE UNIVERSITY, NOTTINGHAM. [*Received, March 25th*, 1958.]

577. *Synthesis of Thiacycloalk-2-enes.*

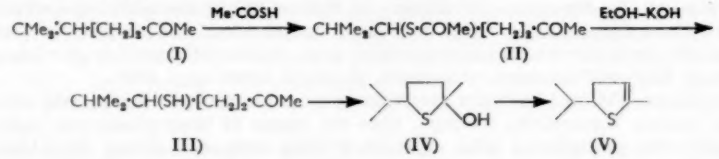
By L. BATEMAN and R. W. GLAZEBROOK.

Substituted thia*cyclo*alk-2-enes have been synthesized by intramolecular condensation of suitably spaced thiol and keto-groups. Attempts to prepare unsubstituted thia*cyclo*alk-2-enes by analogous reactions involving aldehyde groups were unsuccessful.

SULPHURATION of alka-1 : 5-dienes, typified in rubber vulcanization, leads to sulphur-bridged intermolecular compounds and to cyclic sulphides.[1] In order to determine the composition of the latter series (cf. refs 2—4) it became necessary to obtain various thia*cyclo*alkenes so that the effect of unsaturation pattern and substitution on their chemical and spectroscopic properties could be ascertained.

Thia*cyclo*hex-3-enes have previously been obtained by reduction of thia*cyclo*hexan-3-ones and dehydration of the resulting thia*cyclo*hexanols,[5,6] and by deacetylation of 3-acetoxythia*cyclo*hexanes.[7] Thia*cyclo*alk-2-enes have been less readily accessible. Replacement of the oxygen in the corresponding dihydropyran by sulphur at high temperature in the presence of hydrogen sulphide yields impure material,[5,8] and the reduction of thiophens with sodium and liquid ammonia gives rather poor yields of mixtures of thia*cyclo*pent-2- and -3-enes which are difficult to separate.[9] The present paper[10] reports new syntheses of pure thia*cyclo*alk-2-enes in good yields by intramolecular condensation of suitably spaced thiol and keto-groups under acidic or basic conditions. Concurrent polycondensation occurs to an extent varying from system to system.

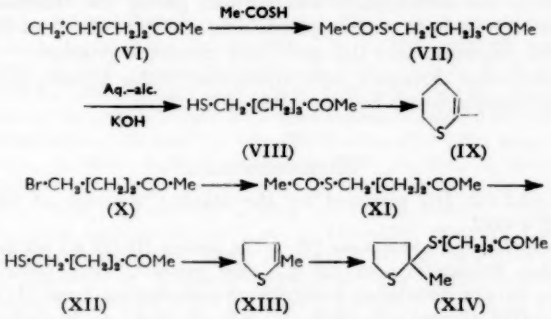
2-Methyl-5-*iso*propylthia*cyclo*pent-2-ene (V) was obtained in 45% overall yield from the common methylheptenone (I) by the annexed reactions:



[1] Farmer and Shipley, *J.*, 1947, 1519.
[2] Glazebrook and Saville, *J.*, 1954, 2094.
[3] Bateman, Glazebrook, Moore, and Saville, Proc. 3rd Rubber Tech. Conf., London, 1954, p. 298.
[4] Bateman, Glazebrook, and Moore, *J.*, 1958, 2846.
[5] Naylor, *J.*, 1949, 2749.
[6] Fehnel and Lackey, *J. Amer. Chem. Soc.*, 1951, **73**, 2473.
[7] Olsen and Rutland, *Chem. Ber.*, 1953, **86**, 361.
[8] Yur'ev, Dubrovina, and Tregubov, *J. Gen. Chem. U.S.S.R.*, 1946, 843.
[9] Birch and McAllan, *J.*, 1951, 2256, 3411.
[10] Cf. Bateman and Glazebrook, *Chem. and Ind.*, 1951, 1093.

Hydrolysis of the ester (II), whose structure follows from the known " abnormal " addition of thiolacetic acid to olefins under the conditions used,[11] gave either the thiol (III) or the dihydrothiophen (V), depending on the severity of the procedure; the possible intermediate (IV) was never isolated.

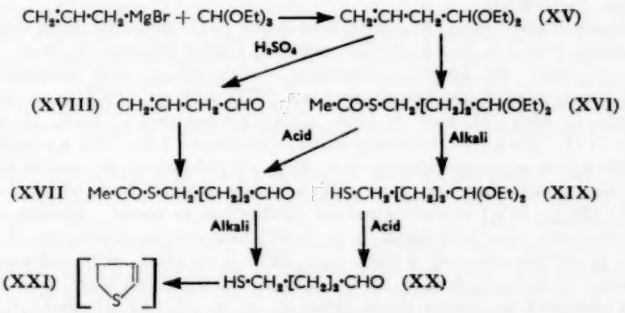
2-Methylthia*cyclo*hex-2-ene (IX) was obtained similarly:



In this case, hydrolysis of the ester (VII) gave the cyclized product (IX) directly, none of the intermediate thiol (VIII) being isolated.

The analogous preparation of 2 : 3-dimethylthia*cyclo*hex-2-ene differs from the previous examples in that the thiol corresponding to (VIII) requires treatment with cold sulphuric acid for dehydration and cyclization.

Unsuccessful attempts were made to apply this synthesis to 2-methylthia*cyclo*pent-2-ene (XIII). The thioester (XI) was obtained in good yield, but on hydrolysis by boiling ethanolic potassium hydroxide or cold dilute methanolic sodium methoxide gave a product which on the basis of elementary analysis, molecular weight, carbonyl content, and absence of thiol function is identified as 2-methyl-2-(4-oxopentylthio)-thia*cyclo*pentane (XIV), which presumably results from interaction of the products (XII) and (XIII) under alkaline conditions. An alternative route to the simple product (XIII)—addition of thiolacetic acid to pent-4-en-2-one—proved impracticable owing to the inaccessibility of this ketone, which could not be prepared by the reaction of dimethylcadmium with but-3-enoyl chloride or of allylmagnesium bromide with acetic anhydride.[12]



The synthesis of thia*cyclo*alk-2-enes unsubstituted at the 2-position by intramolecular condensation of thiol and aldehyde groups could not be realized, partly because of the difficulty of introducing a thiol group into an aldehyde in a suitable position, and partly because of the preferential polymerization of aldehydes under the condition of condensation.

[11] Cunneen, *J.*, 1947, 134.
[12] Newman and Booth, *J. Amer. Chem. Soc.*, 1945, **67**, 154.

XUM

For example, attempts to synthesize thia*cyclo*pent-2-ene (XXI) by the procedures in the reaction scheme failed at different stages.

But-3-enal (XVIII), obtained from of 4 : 4-diethoxybut-1-ene (XV), was readily converted into 4-acetylthiobutanal (XVII), which was unaffected by cold methanolic sodium methoxide and was polymerized in hot ethanolic sodium hydroxide. Addition of thiolacetic acid to the acetal (XV) was normal, giving the thioester (XVI), which partly polymerized on treatment with sulphuric acid and gave the thiol (XIX) on alkaline hydrolysis, but with sulphuric acid this gave only involatile products.

The thia*cyclo*alk-2-enes described were colourless, stable liquids, giving well-defined solid sulphones and sulphidimines by conventional methods.

Experimental

6-Methylhept-5-en-2-one (I), prepared by the alkaline cleavage of citral,[13] had b. p. 65—66°/10 mm., n_D^{20} 1·4412.

2-*Methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* (V).—The ketone (I) (42 g.) reacted exothermically with freshly distilled thiolacetic acid (25 g.); the product, after being warmed on the steam-bath for 1 hr., gave on distillation 5-*acetylthio*-6-*methylheptan*-2-*one* (II) (51 g., 77%), b. p. 134°/10 mm., n_D^{20} 1·4786 (Found: C, 59·3; H, 9·0; S, 15·4. $C_{10}H_{18}O_2S$ requires C, 59·5; H, 8·95; S, 15·75%). Refluxing this thiolester (II) (51 g.) with potassium hydroxide (40 g.) in aqueous ethanol (400 ml.; 50% v/v) for 1 hr. gave 5-*mercapto*-6-*methylheptan*-2-*one* (III), which crystallized as colourless needles [from light petroleum (b. p. <40°)], m. p. 66—68° (C, 59·6; H, 10·0; S, 20·0. $C_8H_{16}OS$ requires C, 60·0; H, 10·0; S, 20·0%). This thiol slowly eliminated water at room temperature. In another experiment, extraction of the hydrolysis product with benzene, followed by distillation, gave 2-*methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* (V) [42·4 g., 45% based on (I)], b. p. 65—67°/10 mm., which on elution through an alumina column with light petroleum (b. p. <40°) had b. p. 63—64°/10 mm., n_D^{20} 1·4932, $\lambda_{max.}$ 2400 Å (ε 2800) (Found: C, 67·5; H, 9·8; S, 22·7. $C_8H_{14}S$ requires C, 67·6; H, 9·8; S, 22·5%). Heating the thiol (III) (5·0 g.) with boric acid (1·0 g.) at 160° for 15 min. gave the product (V) (3·0 g., 68%), b. p. 63°/10 mm., n_D^{20} 1·4933 (Found: C, 67·2; H, 9·8; S, 23·0%). Oxidation of this compound in glacial acetic acid with 30% hydrogen peroxide at room temperature for 2—3 days [14] gave 2-*methyl*-5-iso*propylthia*cyclo*pent*-2-*ene* 1 : 1-*dioxide* as colourless needles [from light petroleum (b. p. 80—100°)], m. p. 66·5—67·5° (Found: C, 55·3; H, 8·2; S, 18·3. $C_8H_{14}O_2S$ requires C, 55·2; H, 8·0; S, 18·4%). Shaking the sulphide (V) with an aqueous solution of chloramine-T gave the *sulphidimine* as colourless prisms (from ethanol), m. p. 120—121° (Found: C, 57·9; H, 6·9; N, 4·5; S, 20·6. $C_{15}H_{21}O_2NS_2$ requires C, 57·9; H, 6·7; N, 4·5; S, 20·6%).

2-*Methylthia*cyclo*hex*-2-*ene* (IX).—Hex-5-en-2-one (VI), prepared from allyl bromide and ethyl acetoacetate,[15] had b. p. 32—33°/10 mm., n_D^{20} 1·4213 (Found: C, 73·3; H, 10·2. Calc. for $C_6H_{10}O$: C, 73·5; H, 10·2%). Reaction of this (98 g.) with thiolacetic acid (76 g.) as described above gave 6-*acetylthiohexan*-2-*one* (VII) (158 g., 91%), b. p. 133°/10 mm., n_D^{20} 1·4812 (Found: C, 55·0; H, 8·0; S, 18·4. $C_8H_{14}O_2S$ requires C, 55·2; H, 8·0; S, 18·7%). The thiolester (VII) (158 g.), on refluxing under nitrogen for 1 hr. with a solution of potassium hydroxide (100 g.) in aqueous ethanol (1 l., 50% v/v), followed by acidification with acetic acid and extraction with benzene, gave a high-boiling product from which 2-*methylthia*cyclo*hex*-2-*ene* (IX) (25 g., 24%) was obtained by distillation *in vacuo*. Elution of this material through alumina with light petroleum (b. p. <40°) followed by distillation of the eluate gave pure (IX), b. p. 50°/10 mm., n_D^{20} 1·5262, $\lambda_{max.}$ 2275 Å (ε 5160), with inflexion at λ 2450 Å (ε 2400) (Found: C, 63·1; H, 9·0; S, 28·1. $C_6H_{10}S$ requires C, 63·2; H, 8·8; S, 28·0%). The *sulphone* was obtained as prisms (from ethanol), m. p. 41—42° (Found: C, 49·3; H, 7·0; S, 21·7. $C_6H_{10}O_2S$ requires C, 49·3; H, 6·85; S, 21·9%). The *sulphidimine derivative* was obtained as needles (from ethanol), m. p. 119·5—120° (Found: C, 55·1; H, 6·2; N, 5·0; S, 22·5. $C_{13}H_{17}O_2NS_2$ requires C, 55·1; H, 6·0; N, 4·95; S, 22·6%).

2 : 3-*Dimethylthia*cyclo*hex*-2-*ene*.—Reaction of ethyl allylacetoacetate with methyl iodide

[13] Cf. Barnard, Bateman, Harding, Koch, Sheppard, and Sutherland, *J.*, 1950, 915.
[14] Barker, Stevens, and Dost, *Rec. Trav. chim.*, 1948, **67**, 451.
[15] Schechter, Green, and LaForge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165.

XUM

in the presence of potassium *tert.*-butoxide gave 3-methylhex-5-en-2-one, b. p. 61°/40 mm., n_D^{20} 1·4241 (Found: C, 74·7; H, 10·8. Calc. for $C_7H_{12}O$: C, 75·0; H, 10·7%). This ketone (46 g.) reacted with thiolacetic acid (35 g.) on irradiation with ultraviolet light for 2 hr. at room temperature, giving *6-acetylthio-3-methylhexan-2-one* (60 g. 78%), b. p. 138—140°/10 mm., n_D^{20} 1·4802 (Found: C, 57·1; H, 8·7; S, 17·4. $C_9H_{16}O_2S$ requires C, 57·5; H, 8·5; S, 17·0%). The thiolester (60 g.) was refluxed under nitrogen for 1 hr. with potassium hydroxide (50 g.) in aqueous ethanol (500 ml.; 50% v/v). The product, on extraction as previously, gave *6-mercapto-3-methylheptan-2-one* (40 g., 90%), b. p. 102—103°/10 mm., n_D^{20} 1·4800 (Found: C, 57·3; H, 9·6; S, 22·1. $C_7H_{14}OS$ requires C, 57·6; H, 9·6; S, 21·9%). Treatment of this thiol (27 g.) with ice-cold sulphuric acid (250 g., 60% w/w) for 1 hr., followed by ether-extraction and distillation of the product, gave 2 : 3-*dimethylthia*cyclo*hex-2-ene* (15 g., 63%). On purification as described above this had b. p. 65—66°/10 mm., n_D^{20} 1·5280, $\lambda_{max.}$ 2280 Å (ε 6840) (Found: C, 65·4; H, 9·5; S, 25·2. $C_7H_{12}S$ requires C, 65·6; H, 9·4; S, 25·0%). The *sulphone* was obtained as needles [from light petroleum (b. p. 60—80°)], m. p. 74·5—75·0° (Found: C, 52·6; H, 7·6; S, 20·2. $C_7H_{12}O_2S$ requires C, 52·4; H, 7·5; S, 20·0%). The *sulphidimine derivative* formed plates (from aqueous ethanol), m. p. 138—139° (Found: C, 56·6; H, 6·5; N, 4·9; S, 21·5. $C_{14}H_{19}O_2NS_2$ requires C, 56·6; H, 6·4; N, 4·7; S, 21·5%).

*Attempted Synthesis of 2-Methylthia*cyclo*pent-2-ene* (XIII).—5-Bromopentan-2-one (X), prepared in a slightly impure state by Boon's method,[16] had b. p. 70·5°/10 mm., n_D^{20} 1·4700 (Found: C, 36·4; H, 5·6; Br, 47·6. Calc. for C_5H_9OBr: C, 36·4; H, 5·5; Br, 48·5%). The bromide (28 g.) was refluxed for 4 hr. with ethanolic sodium thiolacetate [from sodium hydroxide (10 g.), the acid (12 g.), and ethanol (100 ml.)]. Dilution of the product with water, followed by ether-extraction and distillation, gave *5-acetylthiopentan-2-one* (XI) (18 g., 67%), b. p. 116—119°/10 mm., n_D^{20} 1·4890 (Found: C, 52·3; H, 7·7; S, 21·0. $C_7H_{13}O_2S$ requires C, 52·5; H, 7·5; S, 20·0%). This ester (37 g.) was kept overnight in methanol (400 ml.) containing a trace of sodium methoxide, after which the bulk of the solvent was removed, and the residue diluted with water, extracted with ether, and distilled, to give *2-methyl-2-(4-oxopentylthio)thia*cyclo*pentane* (XIV) (15 g., 60%), b. p. 120—122°/0·01 mm., n_D^{20} 1·5324 (Found: C, 55·0; H, 8·4; S, 29·2%; *M*, 212. $C_{10}H_{18}OS_2$ requires C, 55·0; H, 8·3; S, 29·4%; *M*, 218). Its infrared spectrum showed the presence of one C=O group per molecule, the absence of thiol groups, and no detectable C:C-type unsaturation.

*Attempted Synthesis of Thia*cyclo*pent-2-ene* (XXI).—Ethyl orthoformate (60 g.) in ether (100 ml.) with allylmagnesium bromide [from allyl bromide (60 g.) and magnesium (38 g.) in ether (400 ml.)] under reflux for 6 hr. gave 4 : 4-diethoxybut-1-ene (XV) (22 g., 41%), b. p. 40°/10 mm., n_D^{20} 1·4096 (Found: C, 66·6; H, 11·2. Calc. for $C_8H_{16}O_2$: C, 66·7; H, 11·1%). Distillation of this from 2N-sulphuric acid gave an aqueous solution (75% w/w) of but-3-enal (XVIII), identified as the 2 : 4-*dinitrophenylhydrazone derivative* (red plates from ethanol), m. p. 186° (Found: C, 48·0; H, 4·1; N, 22·3. $C_{10}H_{10}O_4N_4$ requires C, 48·0; H, 4·0; N, 22·4%). The aqueous aldehyde (75% w/w; 5·0 g.) reacted exothermically with thiolacetic acid (5·0 g.), to give *4-acetylthiobutanal* (XVII), b. p. 95—96°/10 mm., n_D^{20} 1·4850 (Found: C, 49·0; H, 6·8; S, 21·9. $C_6H_{10}O_2S$ requires C, 49·4; H, 6·8; S, 21·9%). This ester was recovered after being kept overnight in methanol contaning a trace of sodium methoxide; when refluxed for 5 min. under nitrogen with 10% aqueous-ethanolic (50% v/v) sodium hydroxide it yielded an undistillable oil.

Addition of thiolacetic acid (10 g.) during 45 min. to the acetal (XV) (20 g.) at 0° with ultraviolet irradiation gave *4-acetylthio-1 : 1-diethoxybutane* (XVI) (16 g., 52%), b. p. 86°/0·01 mm., n_D^{20} 1·4627 (Found: C, 54·1; H, 9·0; S, 14·8. $C_{10}H_{20}O_3S$ requires C, 54·6; H, 9·1; S, 14·5%), treatment of which with 2N-sulphuric acid failed to give any steam-volatile material, the only isolable products being the unchanged ester (*ca.* 50%) and a non-volatile oil. The ester (21 g.) with potassium hydroxide (20 g.) in aqueous ethanol (50% v/v; 200 ml.) during 2 hr. at room temperature gave 4 : 4-*diethoxybutanethiol* (XIX) (15 g., 88%), b. p. 97°/10 mm., n_D^{20} 1·4515 (Found: C, 53·6; H, 10·1; S, 18·1. $C_8H_{18}O_2S$ requires C, 54·0; H, 10·1; S, 18·0%), whence 2N-sulphuric acid yielded only an undistillable oil.

THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION, 48–56, TEWIN ROAD, WELWYN GARDEN CITY, HERTS.

[*Received, December 23rd*, 1957.]

[16] Boon, B.P. 558,286/1943.

578. *The Reaction of Sulphur and Sulphur Compounds with Olefinic Substances. Part VIII.*[1] *The Reaction of Sulphur with Mono-olefins.*

By L. Bateman, R. W. Glazebrook, C. G. Moore, M. Porter, G. W. Ross, and R. W. Saville.

Reaction of sulphur with mono-olefins at 140° gives, not only alkenyl alkyl polysulphides as previously supposed, but also substantial amounts of more saturated compounds having two attachments of sulphur per olefin moiety. The latter appear to have mainly cyclic structures (derived from the linking of two ethylenic centres) and include polymeric polysulphides (derived from similar linking of three or more olefin units); epithio-groups could not be detected in these polysulphides. The proportion of alkenyl alkyl polysulphide to these other products varies in a regular manner among different types of olefin.

The mechanistic significance of these findings is discussed in Part XI.

Introduction to Parts VIII—XI.—Earlier Parts of this series [1-6] reported the partial separation and identification of the complex products of certain sulphur–olefin and related reactions chosen as models for examining the mechanism of vulcanisation of natural and synthetic rubbers by sulphur. The main conclusion was that sulphur–olefin interaction proceeds by free-radical chain processes, and this has been quoted elsewhere [7] and widely accepted.

Results are now presented which extend and correct the earlier findings and lead to the different mechanistic conclusion that the reactions are *polar* in type, involving heterolysis of S–S and C–H bonds. This paper and Part IX [8] deal with the products of the reactions of sulphur with mono-olefins and a 1 : 5-diolefin, respectively, and Part X [9] presents a complementary kinetic investigation, the first for such reactions. All the experimental evidence is collated in Part XI [10] in a general theory of sulphur–olefin interaction.

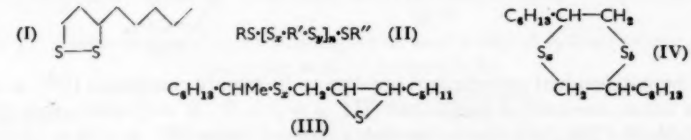
Reaction of Sulphur with Mono-olefins at about 140°.—Previous workers [2,11,12] have reported that the products are mainly polysulphides $R{\cdot}S_x{\cdot}RH_2$ in which the hydrocarbon attachments are alkenyl (R) and alkyl (RH_2), as deduced from elementary analyses and from the results of degradation with ozone.[11] Ozonisation was, however, of limited diagnostic value, since the method was applied before the response of different sulphide units to ozone had been ascertained.[13] The comparable use of methyl iodide [14] is also inadmissible since its reaction with sulphides to yield trimethylsulphonium iodide is non-specific [15] with respect to the structures of R and R′ in R·S·R′ and occurs to negligible extent with di- and poly-sulphides.[16]

[1] Part VII, Farmer, Ford, and Lyons, *J. Appl. Chem.*, 1954, **4**, 554.
[2] Farmer and Shipley, *J.*, 1947, 1519.
[3] Naylor, *J.*, 1947, 1532.
[4] Bloomfield, *J.*, 1947, 1546.
[5] *Idem*, *ibid.*, p. 1547.
[6] *Idem*, *J. Soc. Chem. Ind.*, 1949, **68**, 66.
[7] Flory, "Principles of Polymer Chemistry," Cornell Univ. Press, 1953, p. 454; Burnett, "Mechanism of Polymer Reactions," Interscience Publ. Inc., New York, 1954, p. 89; Grassie, "The Chemistry of High Polymer Degradation Processes," Butterworths, London, 1956, p. 246.
[8] Bateman, Glazebrook, and Moore, following paper.
[9] Ross, Part X, this issue.
[10] Bateman, Moore, and Porter, Part XI, this issue.
[11] Armstrong, Little, and Doak, *Ind. Eng. Chem.*, 1944, **36**, 628.
[12] Selker and Kemp, *ibid.*, 1947, **39**, 895.
[13] Barnard, *J.*, 1957, 4547.
[14] Selker and Kemp, *Ind. Eng. Chem.*, 1944, **36**, 16.
[15] Bloomfield, Proc. 2nd Rubber Tech. Conf., London, 1948, p. 79.
[16] Selker, *Ind. Eng. Chem.*, 1948, **40**, 1467.

The products of the sulphuration of differently substituted alkenes (oct-1-ene, *cyclo*hexene, hept-2-ene, 2-methylpent-2-ene, 1-methyl*cyclo*hexene, and 2 : 6-dimethyloct-2-ene) have now been examined in greater detail, and their structures determined by a combination of conventional analyses, hydrogenolysis by reaction with lithium aluminium hydride,[17] and spectroscopic comparison of original and hydrogenolysis products with synthetic reference compounds.

Reaction of Sulphur with Oct-1-ene.—At 140° complete combination of the sulphur (0·350 g.-atom/mole) occurs in 14 hr. (see also Part X).[9] The product consisted of (i) unchanged olefin, spectroscopically identical with the original material, (ii) a small quantity of a volatile sulphur compound, probably 1 : 2-epithio-octane, and (iii) the main product, " octene polysulphide."

The polysulphide had an average composition $(C_8H_{16\cdot1}S_{2\cdot33})_{2\cdot12}$, apparently indicative of two octene units joined by a polysulphidic link, with the retention of the H : C ratio of the original olefin. The inference that on average one octyl and one octenyl group are present per molecule (cf. refs. 2 and 12) is, however, incorrect since the infrared spectrum showed the polysulphide to be predominantly saturated, there being no vinylic ($CH_2{:}CHR$) unsaturation and a maximum of 0·22 double bond as *trans*-CHR:CHR′ group per molecule. On hydrogenolysis, only 45% of the total sulphur was liberated as hydrogen sulphide (an octenyl octyl polysulphide of the above composition should yield *ca.* 60%), and the remainder was located in (*a*) a monothiol fraction, mainly octane-2-thiol with a minor amount of an unsaturated thiol having *trans*-CHR:CHR′ groups, (*b*) octane-1 : 2-dithiol, (*c*) a monosulphide comprising dioctyl and/or octenyl octyl sulphide, and (*d*) a high-boiling fraction whose analyses indicated formula $(C_8H_{15\cdot6}S_{1\cdot0})_{2\cdot4}$. No evidence for the presence of octane-1 : 3-dithiol could be obtained; oxidation of the dithiol fraction and attempts to detect the formation of the disulphide (I) by the characteristic ultraviolet absorption of the 1 : 2-dithiolan ring system [18] were unsuccessful.



On less complete evidence, it had previously been inferred [19] that the dithiol results from the hydrogenolysis of polymeric polysulphides typified by (II). The observed composition of the bulk polysulphide precludes the presence of appreciable amounts of such structures unless (i) the ebullioscopic method for determining the molecular weight gives an erroneously low value, or (ii) products of low molecular weight, containing only one olefinic unit per molecule, are also present. Both these possibilities have been investigated and must be dismissed: the ebullioscopic method shows no anomalous features when applied to authentic di- and poly-sulphides, and fractionation of the total polysulphide yields no material containing single olefin units. Further, the relative molar yield of mono- and di-thiols of 1·1 : 1 is incompatible with their derivation from a structure (II). The dithiol could result from hydrogenolysis of an alkenyl alkyl structure $C_8H_{17}{\cdot}S_z{\cdot}C_8H_{15}$ (one double bond), followed by combination of the hydrogen sulphide and octenethiol produced, but this would be at variance with the spectroscopic data, and with negative results from experiments to test the formation of dithiols by secondary reactions during the hydrogenolysis of authentic alkenyl alkyl and dialkenyl polysulphides. Thus, the hydrogenolysis of di(*cyclo*hex-2-enyl) polysulphide gives solely hydrogen sulphide and *cyclo*hex-2-ene-1-thiol.

[17] Arnold, Lien, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 731; Moore and Saville, *J.*, 1954, 2082.
[18] Barltrop, Hayes, and Calvin, *J. Amer. Chem. Soc.*, 1954, **76**, 4348.
[19] Bateman, Glazebrook, Moore, and Saville, Proc. 3rd Rubber Tech. Conf., London, 1954, p. 298.

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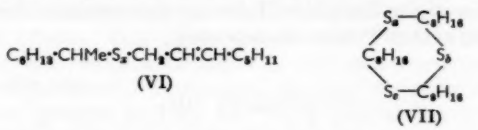
The only remaining explanation is that the dithiol is primarily derived from products composed of two hydrocarbon units joined by sulphur bridges in such a way that one or both units have more than one sulphur attachment, *i.e.* (III) or (IV). On hydrogenolysis, a compound (IV) would yield only the observed octane-1 : 2-dithiol, but a compound (III) would be expected to give the 1 : 2- and the 1 : 3-isomers unless scission of the epithio-ring is specifically oriented. Such orientation is unlikely, and positive evidence favouring structure (IV) has been obtained by treating the polysulphide with potassium hydrogen sulphide. A product (V), $(C_8H_{16\cdot1}S_{1\cdot4})_3$, resulted, which was practically free from thiol groups and polysulphide units greater than S_2. Hydrogenolysis of product (V) yielded a C_8 thiol, octane-1 : 2-dithiol, dioctyl and/or octenyl octyl sulphide, and a polymer $(C_8H_{15\cdot3}S_{1\cdot1})_{3\cdot6}$, *i.e.*, products similar to those obtained likewise from the parent polysulphide. The observed transformations are consistent with the attack of HS^- ions on the S–S bonds in compound (IV), but not with attack on a structure (III), which would give, *inter alia*, a product containing free thiol groups, disulphide or shortened polysulphide linkages, and hydrocarbon units with three sulphur atoms directly attached to them, and on hydrogenolysis would give either an octanetrithiol or a dimercaptodioctyl monosulphide. Evidence based on other related aspects of episulphide reactivity [20] is also against the presence of compound (III).

The monosulphide and the high-boiling fraction (*d*) obtained after hydrogenolysis of the parent octene polysulphide (p. 2839) appear to be original constituents of the latter and not derived products. The monosulphide is dioctyl sulphide and/or octenyl octyl sulphide, formation of the former paralleling that of di*cyclo*hexyl sulphide in the corresponding sulphuration of *cyclo*hexene.[2] The fraction (*d*), $(C_8H_{15\cdot6}S_{1\cdot0})_{2\cdot4}$, on the basis of its predominantly saturated nature, its low thiol content, and its resistance to hydrogenolysis



(confirmed by independent experiment) appears to be mainly compound (IV; $a = b = 1$), mixed with minor amounts of compound (II; $x = y = 0$; $n = 1$) and a mercaptomonosulphide, $C_8H_{17}\cdot S\cdot C_8H_{16}\cdot SH$, the latter being derived from (II; $x = 0$, $y \geqslant 1$; $n = 1$). The resistance of the C–S bonds in compounds (IV; $a = b = 1$) and (II; $x = y = 0$; $n = 1$) to hydrogenolysis is comparable with the resistance of C–S bonds in monosulphides and in the polymer $(C_8H_{16}S)_n$ obtained from 1 : 2-epithio-octane.[20]

After allowance for loss on isolation, the yields of hydrogenolysis products recorded in Table 1 allow a semi-quantitative analysis of the octene polysulphide to be made as follows: octenyl octyl polysulphide (VI; $x = 6{\cdot}7$), 25 mole %; (IV; $a + b = 6{\cdot}7$), 30 mole %; dioctyl- and/or octenyl octyl sulphide, 15 mole %; (II; $R = R' = R'' = C_8$; $x + y = 4{\cdot}7$, $n = 1$), 15 mole %; and a mixture of (IV; $a = b = 1$) and (II; $R = R' = R'' = C_8$; $x = y = 0$, $n = 1$), 15 mole %. The elementary analysis and bulk unsaturation of this mixture agree with the above values. Similarly, the product (V) obtained on reaction with hydrosulphide (see above) appears to consist of compounds: (II; $R = R' = R'' = C_8$; $x + y = 3{\cdot}9$; $n = 1$), 15 mole %; (II; $R = R' = R'' = C_8$; $x + y = 1{\cdot}95$; $n = 2$), 25 mole %; dioctyl and/or octenyl octyl sulphide, 30 mole %; (VII; $a + b + c = 5{\cdot}9$), 25 mole %; and non-reducible material $(C_8H_{15\cdot3}S_{1\cdot1})_{3\cdot6}$, 5 mole %. This composition fulfils the analytical requirements and is also in accord with the derivation of (V) from the parent polysulphide.

The above structures, while in agreement with the hydrogenolysis and analytical data, are to some extent arbitrary in respect of molecular complexity and length of the polysulphide linkage. The compositions detailed above should be regarded as typifying the

[20] Moore and Porter, *J.*, 1958, 2062.

relative contributions of the various generic structures whose presence is experimentally well founded.

TABLE 1. *Yields of hydrogenolysis products from octene polysulphide and the sulphurated product* (V) *(mole per mole of reactant).*

Reactant	H_2S	Mono-thiol	Di-thiol	Mono-sulphide	Residue	Recovery (wt. %)
$(C_8H_{16\cdot1}S_{2\cdot33})_{2\cdot12}$	2·3	0·62	0·60	0·15	0·17 *	90
(V); $(C_8H_{16\cdot1}S_{1\cdot4})_3$	0·16	0·71	1·25	0·30	0·05 †	94

* Average composition $(C_8H_{15\cdot8}S_{1\cdot0})_{2\cdot4}$. † Average composition $(C_8H_{15\cdot2}S_{1\cdot1})_{2\cdot4}$.

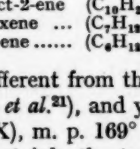
Reaction of Sulphur with sym.*-Dialkyl- and Trialkyl-ethylenes.*—The average compositions of polysulphides formed from these olefins conform to the pattern observed with oct-1-ene, *viz.*, the major constituents consist of two hydrocarbon units joined by either one or two chains of sulphur atoms, with the C : H ratio of the parent olefin retained (Table 2). Likewise, spectroscopic examination reveals that the total unsaturation present is in all cases less than is required for alkenyl alkyl structures. The residual unsaturation of the several polysulphides is not uniform, however, and varies in the order: 2-methylpent-2-ene > 1-methyl*cyclo*hexene > *cyclo*hexene > hept-2-ene > oct-1-ene. (2 : 6-Dimethyloct-2-ene is not included in this series as the spectroscopic analysis is less accurate.)

Hydrogenolysis of the polysulphides gave hydrogen sulphide, mono- and di-thiols containing one olefin unit per molecule, and higher-boiling material containing sulphur-groups resistant to lithium aluminium hydride. The following conclusions can be drawn about the nature of these products: (i) the monothiols are partly unsaturated; (ii) the saturated monothiols derived from the polysulphides of the trialkylethylenes are tertiary; in no case has the secondary isomer been identified; (iii) the dithiols are saturated, and by analogy with the formation of octane-1 : 2-dithiol from " octene polysulphide " are believed to have the thiol groups on vicinal carbon atoms. The dithiol obtained from " *cyclo*hexene polysulphide " gave on treatment with benzaldehyde a phenyldithiolan, m. p.

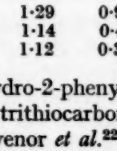
TABLE 2. *Compositions of olefin polysulphides, and yields of hydrogenolysis products (mole per mole of polysulphide).*

Polysulphide from	Formula	Mono-thiol	Dithiol	Molar ratio mono- to di-thiol	H_2S	Residue	Recovery (wt. %)
Oct-1-ene	$(C_8H_{16\cdot1}S_{2\cdot33})_{2\cdot12}$	0·62	0·60	1·1 : 1	2·3	0·32	90
*cyclo*Hexene	$(C_6H_{9\cdot8}S_{2\cdot67})_{2\cdot1}$	0·90	0·53	1·67 : 1	—	0	63
Hept-2-ene	$(C_7H_{14\cdot0}S_{2\cdot77})_{2\cdot3}$	—	—	—	—	—	—
2 : 6-Dimethyloct-2-ene	$(C_{10}H_{20\cdot7}S_{2\cdot8})_{2\cdot18}$	1·29	0·90	1·47 : 1	2·88	0	~100
1-Methyl*cyclo*hexene ...	$(C_7H_{12\cdot0}S_{2\cdot63})_{2\cdot17}$	1·14	0·42	2·3 : 1	2·90	0·12	84
2-Methylpent-2-ene	$(C_6H_{12\cdot0}S_{2\cdot16})_{2\cdot06}$	1·12	0·31	3·7 : 1	2·30	0·05	84

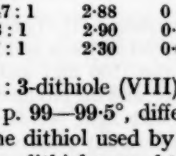
133—134°, different from the hexahydro-2-phenylbenzo-1 : 3-dithiole (VIII), m. p. 115·5° (see Culvenor *et al.*[21]), and yielded a trithiocarbonate, m. p. 99—99·5°, different from the compound (IX), m. p. 169° (see Culvenor *et al.*[22]). As the dithiol used by these authors was almost certainly the *trans*-form, it is inferred that the dithiol now obtained is *cyclo*hexane-*cis*-1 : 2-dithiol.



(VIII)



(IX)



(X)

The above findings indicate that the polysulphides listed in Table 2 are composed of constituents similar in type to those present in octene polysulphide, *viz.*, alkenyl alkyl

[21] Culvenor and Davies, *Austral. J. Sci. Res.*, 1948, **1**, *A*, 236.
[22] Culvenor, Davies, and Pausacker, *J.*, 1946, 1050.

polysulphides, cyclic structures (X; R = R′ = alkyl; R″ = H or alkyl; R‴ = H) analogous to (IV), and polymeric compounds (II). The yields of hydrogen sulphide, mono- and di-thiols, and non-reducible sulphur-compounds obtained on hydrogenolysis (Table 2) show that the polysulphides from the di- and tri-alkylethylenes contain a higher proportion of the alkenyl alkyl polysulphide and a lower proportion of the cyclic and polymeric structures, (X) and (II), respectively, than the products from oct-1-ene. The order in which the alkenyl alkyl polysulphides are formed preferentially is: 2-methylpent-2-ene > 1-methyl*cyclo*hexene > *cyclo*hexene > 2 : 6-dimethyloct-2-ene > oct-1-ene, which parallels the order of retention of the olefinic unsaturation in the bulk sulphurated product. As for " octene polysulphide," it is possible to calculate the approximate compositions of those polysulphides for which the product recovery on hydrogenolysis approached 100% (Table 3).

Olefinic Structure of the Polysulphides.—Spectroscopic examination of the " octene polysulphide " shows that the unsaturation present is wholly of the type CHR:CHR′, there

TABLE 3. *Approximate compositions of bulk polysulphides (mole fraction).*

Polysulphide from	Alkyl-S_x-alkenyl	(X)	(II)	RSR′	Residual material	Value of x $(a + b)$
2-Methylpent-2-ene	0·80	0·15	0	—	0·05	$4{\cdot}5_5$
1-Methyl*cyclo*hexene	0·60	0·20	0·10	—	0·10	6·1
2 : 6-Dimethyloct-2-ene ...	0·45	0·35	0·20	—	—	6·0
Oct-1-ene	0·25	0·30	0·15	0·15	0·15	6·7

being none of the vinylic type of the parent olefin; only *trans*-CHR:CHR′ groups have been identified, but the *cis*-isomer cannot be definitely excluded on the available evidence. This complete double-bond shift is a special feature of the oct-1-ene system which is not observed with the other unsymmetrical olefins studied. The polysulphides from the trialkylethylenes show only minor changes in unsaturation type, there being only small amounts of the CHR:CHR′ and CH_2:CRR′ forms present. Ultraviolet spectra show the absence of vinyl sulphide groups, C=C·S_x·.

EXPERIMENTAL

Preparation of Materials.—Sulphur was purified by Bacon and Fanelli's method.[23] Oct-1-ene and hept-2-ene were Phillips Petroleum Company " Pure Grade " materials. The other olefins were prepared by standard methods and were analytically and spectroscopically pure.

General Procedures—(1) *Hydrogenolysis of polysulphides.* The polysulphide (10 g.) in dry tetrahydrofuran (50 ml.) was added slowly with stirring to lithium aluminium hydride (3—5 g.) in tetrahydrofuran (100 ml.) and the mixture refluxed for 4—6 hr. Excess of reagent was destroyed with ice, and the products were hydrolysed with 2N-sulphuric acid (200 ml.). The thiols were extracted with light petroleum, the extract was washed with water and dried (Na_2SO_4), the solvent was carefully removed through a column, and the thiols were fractionated.

(2) *Determination of " removable sulphur " in polysulphides.* " Removable sulphur," defined as the percentage of total sulphur in the polysulphide liberated as hydrogen sulphide by hydrogenolysis with lithium aluminium hydride, was determined as previously described.[1]

(3) *Determination of thiols.* The thiol (10—20 mg.) in aqueous ethanol (100 ml., 95%) was titrated against aqueous 0·01N-silver nitrate and the end-point determined by the amperometric method.[24]

(4) 2 : 4-*Dinitrophenyl sulphide derivatives of thiols.* These were prepared by the method of Bost, Turner, and Norton.[25]

(5) Molecular weights were determined ebullioscopically in benzene.

[23] Bacon and Fanelli, *Ind. Eng. Chem.*, 1942, **34**, 1043.
[24] Kolthoff and Harris, *Ind. Eng. Chem. Analyt.*, 1946, **18**, 161.
[25] Bost, Turner, and Norton, *J. Amer. Chem. Soc.*, 1932, **54**, 1985.

(6) *Spectrometric analysis.* Infrared spectra were recorded on a Grubb-Parsons single-beam spectrometer with a rock-salt or lithium fluoride prism, or on a Hilger H.800 spectrometer. Ultraviolet absorption spectra were determined in ethanol or *cyclo*hexane with a Hilger Uvispek spectrophotometer. Unsaturated groups were identified by the characteristic bands of the olefinic ν(C:C) and δ(CH) vibrations,[26] and (unless stated otherwise) were estimated in CCl_4 or CS_2 solution by reference to the absorption characteristics of the δ(CH) band of relevant olefins. Identification of the types of C–S linkages in the polysulphides and their hydrogenolysis products was based on the infrared spectroscopic characteristics of synthetic thiols, sulphides, and polysulphides. The absence of conjugated olefinic unsaturation was based on the absence of absorption at ~2400 Å; the absence of the C=C·S_x-chromophore in the polysulphides was established by comparison of their ultraviolet absorption characteristics with those of authentic saturated and unsaturated mono- and poly-sulphides.

Reaction of Oct-1-ene with Sulphur.—This is described in detail as illustrative of the procedure used with all the olefins listed on p. 2839. The olefin (101·6 g.) and sulphur (10·16 g.) were heated together *in vacuo* at 140° ± 0·1° for 14·0 hr. No sulphur was deposited from the product during 24 days at −20°. Evaporative distillation of the product at $<50°/<10^{-3}$ mm. gave: (i) unchanged olefin (83·09 g.), n_D^{20} 1·4092 (Found: C, 85·5; H, 14·3%), which contained only CH_2:CHR groups and was devoid of conjugated unsaturation; (ii) a volatile fraction (3·10 g.) which was fractionated further into (ii*a*) oct-1-ene (2·10 g.), n_D^{20} 1·4095 (Found: C, 85·8; H, 14·2; S, 0·2%), and (ii*b*) a yellow liquid (0·42 g.) (Found: C, 66·6; H, 10·8; S, 21·9; thiol-S, 0·4. Calc. for $C_8H_{16}S$: C, 66·6; H, 11·2; S, 22·2%), which was predominantly saturated, devoid of thiol and thio-ketone groups, and shown by infrared spectral analysis to be mainly 1 : 2-epithio-octane; and (iii) " octene polysulphide " (24·84 g.), a dark brown liquid residue, n_D^{20} 1·5611 [Found: C, 51·4, 51·7; H, 8·6, 8·8; S, 40·0, 40·3; " Removable sulphur," 44·8, 45·3%; *M*, 412, 410. Corresponds to $(C_8H_{16\cdot1}S_{2\cdot33})_{2\cdot12}$], which was largely saturated.

The polysulphide (iii) (10·02 g.) with lithium aluminium hydride (4·76 g.) gave the following thiol fractions: (iii*a*) b. p. 71—75°/17 mm., n_D^{20} 1·4564 (2·09 g.) (Found: C, 66·0; H, 12·0; S, 21·9; thiol-S, 22·6; C : H, 8 : 17·3. Calc. for $C_8H_{16}S$: C, 66·6; H, 11·2; S, 22·2. Calc. for $C_8H_{18}S$: C, 65·7; H, 12·4; S, 21·9%); (iii*b*) b. p. 75—110°/17 mm., n_D^{20} 1·4817 (0·26 g.) (Found: thiol-S, 30·8%); (iii*c*) b. p. 55—56°/0·08 mm., n_D^{20} 1·5004 (2·12 g.) (Found: C, 54·5; H, 10·3; S, 35·9; thiol-S, 36·4, 36·6; C : H, 8 : 18·0. Calc. for $C_8H_{18}S_2$: C, 53·95; H, 10·15; S, 35·95%); (iii*d*) b. p. 56—110°/0·08 mm., n_D^{20} 1·4779 (1·29 g.) (Found: C, 67·6; H, 12·0; S, 20·6; thiol-S, 12·9, 13·2%; *M*, 220, 240. Calc. for 43 : 57 mole % mixture of octanedithiol and dioctyl sulphide; C, 67·4; H, 12·2; S, 20·4; thiol-S, 12·3%; *M*, 224); and (iii*e*) a residue, n_D^{20} 1·5075 (1·42 g.) [Found: C, 65·3; H, 10·7; S, 22·2; thiol-S, ~6%; *M*, 330, 360. Corresponds to $(C_8H_{15\cdot6}S_{1\cdot92})_{2\cdot39}$].

Examination of the hydrogenolysis fractions. Fraction (iii*a*) was mainly saturated, although absorption at 967 cm.$^{-1}$ could be due to up to 0·20 double bond as *trans*-CHR:CHR′ group per mole. Fraction (iii*a*) gave a 2 : 4-dinitrophenyl sulphide which was separated chromatographically into: (*a*) 2 : 4-dinitrophenyl 1-methylheptyl sulphide, m. p. and mixed m. p. 44—45° (Found: C, 53·7; H, 6·3; N, 8·9. Calc. for $C_{14}H_{20}O_4N_2S$: C, 53·8; H, 6·5; N, 9·0%), having an infrared spectrum identical with that of the synthetic material; and (*b*) an orange-red oil (Found: C, 52·1; H, 6·15; N, 9·1%) which crystallised after 3 months to give 2 : 4-dinitrophenyl 1-methylheptyl sulphide, m. p. and mixed m. p. 46—48°.

The dithiol fraction (iii*c*) was saturated, weak absorption at 967 cm.$^{-1}$ being attributed to a skeletal vibration also observed in the spectrum of octane-1 : 2-dithiol. The dithiol was identified as octane-1 : 2-dithiol by formation of the bis-2 : 4-dinitrophenyl sulphide which was separated chromatographically into two forms (from ethanol–acetone) having m. p.s and mixed m. p.s 58—60° (Found: C, 46·9; H, 4·35; N, 10·9, 10·8. Calc. for $C_{20}H_{22}O_8N_4S_2$: C, 47·1, H, 4·3; N, 11·0%) and 95—97·5° (Found: C, 47·1; H, 4·5; N, 10·7, 10·9%). Recrystallisation of the two forms from acetone at −78° gave the form of m. p. 39—40°, and recrystallisation from ethanol–acetone gave other forms, m. p. 61—62·5° and 70·5—72°.

Fractions (iii*d*) and (iii*e*) were largely saturated; fraction (iii*d*) contained a saturated dithiol, but other constituents were not identified (conjugated structures were absent).

Hydrogenolysis of fraction (iii*e*) (1·05 g.) gave hydrogen sulphide (equiv. to 0·4% of " removable sulphur ") and the following fractions: (iii*ei*) b. p. $< 99°/10^{-2}$ mm. (0·08 g.) (Found: C, 62·0; H, 10·8; S, 25·5%); (iii*eii*) b. p. 99—100°/10^{-2} mm. (0·306 g.) (Found: C, 65·9; H,

[26] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, pp. 31 *et seq.*

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11·3; S, 22·15%; *M*, 249, 277. Calc. for $C_{16}H_{34}S_3$: C, 66·1; H, 11·8; S, 22·1%; *M*, 291. Calc. for $C_{16}H_{32}S_2$: C, 66·6; H, 11·2; S, 22·2%; *M*, 289), which showed no infrared absorption in the 6μ region but slight absorption at 970 cm.$^{-1}$ which could be due to 0·13 *trans*-CHR:CHR′ group per mole, whilst the presence of 1·1—1·4 thiol groups per mole was also indicated, and (iiiciii) a residue (0·51 g.) (Found: C, 68·4; H, 10·4; S, 19·3%; *M*, 569, 576) which was mainly saturated and devoid of thiol groups.

*Absence of octane-*1 : 3*-dithiol in the hydrogenolysis fraction* (iiic). Fraction (iiic) (0·879 g.) in light petroleum (40 ml.) was oxidised with excess of iodine in aqueous potassium iodide. The final excess of iodine was destroyed, the organic layer separated, washed with water, and dried (Na_2SO_4), and the solvent removed *in vacuo*, to give a *disulphide polymer* (0·700 g.) [Found: C, 57·2; H, 9·8; S, 32·7%; *M*, 710, 737, 745. $(C_8H_{16}S_2)_4$ requires C, 54·2; H, 9·7; S, 36·1%; *M*, 705] which showed no ultraviolet absorption maximum at 3300 Å. Comparable oxidation of octane-1 : 2-dithiol (0·886 g.) gave a disulphide polymer (0·740 g.) (Found: C, 56·0; H, 9·4; S, 34·7%; *M*, 947, 1015) showing no maximum absorption at 3300 Å. Oxidation of propane-1 : 3-dithiol in light petroleum gave 1 : 2-dithiolan having maximum absorption at 3270—3280 Å. Comparable results to the above were obtained by partial aerobic oxidation of *dilute* ethanolic solutions of fraction (iiic) and propane-1 : 3-dithiol.

*Reaction of "Oct-*1*-ene Polysulphide" with Potassium Hydrogen Sulphide.*—The polysulphide (iii) [Found: C, 52·15; H, 8·65; S, 39·6%; *M*, 427, 405. Corresponds to $(C_8H_{15\cdot8}S_{2\cdot28})_{2\cdot25}$] (8·23 g.) was shaken for 48 hr. at room temperature with an ethanolic solution of potassium hydrogen sulphide [prepared by saturating a solution of potassium hydroxide (7·1 g.) in ethanol (78 ml.) with hydrogen sulphide at 0°]. Ethanol was removed under reduced pressure, and the product treated with water (200 ml.) and extracted with light petroleum (3 × 75 ml.). Acidification of the aqueous portion with dilute hydrochloric acid gave sulphur (1·37 g., corresponding to 42% of "removable sulphur") but no organic material. Removal of the solvent from the light petroleum extract gave a dark brown liquid (V) (6·76 g.), n_D^{20} 1·523 [Found: C, 60·9; H, 10·3; S, 29·2; thiol-S, 0·3; "removable sulphur," 3·9%; *M*, 463, 470. Corresponds to $(C_8H_{14\cdot1}S_{1\cdot41})_{2\cdot97}$], which was devoid of thiol groups and predominantly saturated; absorption at 970 cm.$^{-1}$ could correspond to a maximum of 0·17 *trans*-CHR:CHR′ unit per molecule. The polysulphide (5·04 g.) with lithium aluminium hydride (1·0 g.) gave the following thiol fractions: (1) b. p. 65—70°/15 mm., n_D^{20} 1·4508 (0·995 g.) (Found: C, 66·6, 67·2; H, 12·3, 12·5; S, 20·0, 20·15; thiol-S, 22·3. Calc. for $C_8H_{16}S$: C, 66·6; H, 11·2; S, 22·2; thiol-S, 22·2. Calc. for $C_8H_{18}S$: C, 65·7; H, 12·4; S, 21·9; thiol-S, 21·9%); (2) b. p. < 50°/0·08 mm. (0·10 g.); (3) b. p. 56—57°/0·08 mm., n_D^{20} 1·4953 (2·025 g.) (Found: C, 54·7; H, 10·2; S, 35·7; thiol-S, 35·4. Calc. for $C_8H_{18}S_2$: C, 53·95; H, 10·15; S, 35·95; thiol-S, 35·95%); (4) b. p. 60—80°/0·01 mm. (0·07 g.); (5) b. p. 80—100°/0·01 mm., n_D^{20} 1·4811 (1·12 g.) [Found: C, 67·8; H, 11·8; S, 20·4; thiol-S, 9·2%; *M*, 245, 256. Corresponds to $(C_8H_{16\cdot6}S_{0\cdot90})_{1\cdot77}$. Calc. for 38 : 62 mole % mixture of octanedithiol and dioctyl sulphide: C, 68·1; H, 12·4; S, 19·5; thiol-S, 10·8%; *M*, 228); (6) a residue, n_D^{20} 1·525 (0·30 g.) [Found: C, 64·2; H, 10·3; S, 23·6%; *M*, 510, 543. Corresponds to $(C_8H_{15\cdot3}S_{1\cdot10})_{3\cdot58}$]. The infrared spectra of fractions (1), (3), (5), and (6) closely resembled those of the corresponding fractions from the hydrogenolysed unchanged polysulphide with the exception that *all* fractions were predominantly saturated.

*Evaporative Distillation of "Oct-*1*-ene Polysulphide."*—Distillation of the polysulphide $(C_8H_{15\cdot8}S_{2\cdot28})_{2\cdot25}$ (1·986 g.) at 100°/10^{-3} mm. in a pot-type "molecular still" [12] gave (1) an orange liquid (0·231 g.) (Found: C, 66·1; H, 11·2; S, 22·45%; *M*, 269, 257. Calc. for $C_{16}H_{32}S_2$: C, 66·6; H, 11·2; S, 22·2%; *M*, 289. Calc. for $C_{16}H_{34}S_2$: C, 66·1; H, 11·8; S, 22·1%; *M*, 291), and (2) an orange liquid (0·121 g.) (Found: *M*, 376, 343). Distillation was continued at 10^{-5} mm. (bath-temp. up to 115°) to give fractions (3) an orange liquid (0·598 g.) [Found: C, 47·9; H, 8·3; S, 43·7%; *M*, 493, 450. Corresponds to $(C_8H_{14\cdot5}S_{3\cdot74})_{2\cdot4}$], (4) an orange-brown liquid (0·429 g.) [Found: C, 47·45; H, 8·1; S, 44·7%; *M*, 520, 483, 462. Corresponds to $(C_8H_{14\cdot3}S_{3\cdot82})_{2\cdot4}$], and (5) a dark brown residue (0·352 g.) [Found: C, 54·05; H, 9·8; S, 36·6%; *M*, 843, 800. Corresponds to $(C_8H_{17\cdot3}S_{2\cdot93})_{4\cdot6}$]. Recovery of the polysulphide was 87%. All fractions were spectroscopically similar to the parent polysulphide.

*Synthesis of Reference Compounds for the Oct-*1*-ene Reaction.*—(1) *Octane-*1*-thiol* (cf. Brown, Jones, and Pinder [27]). 1-Acetylthio-octane, b. p. 116—117°/10 mm., n_D^{20} 1·4641 (64%) (Found: C, 63·7; H, 10·6; S, 16·8. Calc. for $C_{10}H_{20}OS$: C, 63·9; H, 10·65; S, 17·0%), was prepared

[27] Brown, Jones, and Pinder, *J.*, 1951, 2123.

by addition of thiolacetic acid to oct-1-ene. Hydrolysis of the thiolester with aqueous-ethanolic potassium hydroxide under nitrogen gave octane-1-thiol, b. p. 77—78°/10 mm., n_D^{20} 1·4542 (85%) (Found: C, 65·65; H, 12·2; S, 21·2. Calc. for $C_8H_{18}S$: C, 65·7; H, 12·4; S, 21·9%). The 2 : 4-dinitrophenyl octyl sulphide had m. p. 75—76° [from light petroleum (b. p. 60—80°)] (Found: C, 54·2, 54·1; H, 6·5, 6·4; N, 9·15. Calc. for $C_{14}H_{20}O_4N_2S$: C, 53·9; H, 6·4; N, 9·0%) (Brown *et al.* report m. p. 78°). The mercuric salt crystallised as plates (from ethanol), m. p. 71—72° (Found: C, 39·15; H, 6·95. Calc. for $C_{16}H_{34}S_2Hg$: C, 39·1; H, 6·95%).

(2) *Octane-2-thiol.* This thiol, b. p. 64—65°/10 mm., n_D^{20} 1·4506 (79%) (Found: C, 66·1; H, 12·4; S, 20·7%), was prepared from 2-bromo-octane and thiourea by the normal method.[28] It gave 2 : 4-dinitrophenyl 1-methylheptyl sulphide, m. p. 44·5—45° (from ethanol) (Found: C, 53·75; H, 6·3; N, 8·8%) (Norman, LeSuer, and Mastin [29] report m. p. 47·5°).

(3) *Octane-1 : 2-dithiol.* A solution of potassium ethyl xanthate (33·6 g.) in acetone (700 ml.) was filtered from insoluble material and then added with stirring during 1 hr. to 1 : 2-dibromo-octane (19·0 g.; b. p. 53—56°/0·15 mm.; n_D^{20} 1·4969) in acetone (35 ml.). The product was filtered, the solvent removed, the yellow residue dissolved in chloroform (50 ml.), washed with water, and dried (Na_2SO_4), and the solvent removed under reduced pressure. The resulting xanthic ester in dry tetrahydrofuran (50 ml.) was hydrogenolysed for 4 hr. by lithium aluminium hydride (7·6 g.) in refluxing tetrahydrofuran (75 ml.) (cf. Djerassi *et al.*[30]), to give *octane-1 : 2-dithiol* (4·3 g., 35%), b. p. 56—59°/0·05—0·1 mm., n_D^{20} 1·4981 (Found: C, 54·0; H, 10·1; S, 36·1; thiol-S, 35·1. $C_8H_{18}S_2$ requires C, 53·95; H, 10·15; S, 35·95; thiol-S, 35·95%). The dithiol showed a weak infrared band at 967 $cm.^{-1}$. The *bis-2 : 4-dinitrophenyl sulphide* exhibited polymorphism, being obtained in a number of forms whose colour and m. p. depended on the conditions of crystallisation. Thus, slow crystallisation from dilute ethanol–acetone solution gave a pale yellow solid, m. p. 56—57°, whereas more concentrated solutions gave deep yellow crystals, m. p. within the ranges 97—98°, 92—94°, and 70—72°. Satisfactory analyses were obtained for all forms (*e.g.*, form of m. p. 97—98°: Found: C, 47·0; H, 4·3; N, 10·95. $C_{20}H_{22}O_8N_4S_2$ requires C, 47·1; H, 4·3; N, 11·0%). Crystallisation from concentrated acetone solutions at −78° gave a form, m. p. 38—38·5°, which changed in 1 month into the form, m. p. 71·5—73°. Attempted preparation of other derivatives of the dithiol for diagnostic purposes was unsuccessful; the bis-(2 : 4-dinitrophenyl sulphone) was unstable, and the trithiocarbonate and benzylidene derivative were oils.

Reaction of Sulphur with Di- and Tri-alkylethylenes.—The olefin and sulphur (10% w/w) were heated together *in vacuo* at 140° for 5 hr. The products were isolated and examined as described above for the oct-1-ene–sulphur reaction. The major experimental findings are summarised in Tables 2 and 3 and in the text (pp. 2841—2).

Synthesis of Reference Compounds.—(1) *Di*(cyclo*hex-2-enyl*) *polysulphide.* Reaction of *cyclo*hex-2-enethiol (7·0 g., b. p. 44—46°/10 mm.) with sulphur (3·0 g.) in the presence of a trace of diethylamine at room temperature gave the polysulphide (8·0 g.) [Found: C, 48·3; H, 5·95; S, 45·8; "removable sulphur," 47·0%; *M*, 300, 316. Corresponds to $(C_6H_{8\cdot9}S_{2\cdot14})_{2\cdot03}$]. Hydrogenolysis of the polysulphide (5·0 g.) yielded only hydrogen sulphide and *cyclo*hex-2-enethiol (2·93 g.), b. p. 48—50°/10 mm., n_D^{20} 1·5242 (Found: C, 63·3; H, 8·8; S, 27·8. Calc. for $C_6H_{10}S$: C, 63·1; H, 8·8; S, 28·1%).

(2) 2 : 6-*Dimethyloctane-2-thiol.* 2-Benzylthio-2 : 6-dimethyloctane (74%; b. p. 100—112°/0·01 mm., n_D^{20} 1·5147) was prepared by the sulphuric acid-catalysed addition of toluene-ω-thiol to 2 : 6-dimethyloct-2-ene (cf. ref. 31). Reduction of the sulphide with sodium in liquid ammonia (cf. ref. 31) gave 2 : 6-*dimethyloctane-2-thiol* (91%), b. p. 84—85°/10 mm., n_D^{20} 1·4543 (Found: C, 68·9; H, 12·65; S, 18·35. $C_{10}H_{22}S$ requires C, 69·0; H, 12·6; S, 18·4%).

(3) 2 : 6-*Dimethyloctane-3-thiol.* 2 : 6-Dimethyloct-2-ene (14 g.) reacted exothermically with mercaptoacetic acid (10 ml.) under ultraviolet light to give 3-acetylthio-2 : 6-dimethyloctane, b. p. 117—118°/10 mm., n_D^{20} 1·4670 (18·5 g., 86%) (Found: C, 66·1; H, 11·05; S, 15·35. Calc. for $C_{12}H_{24}OS$: C, 66·7; H, 11·1; S, 14·8%). Hydrolysis of the thiolester (18·4 g.) with boiling aqueous-ethanolic potassium hydroxide during 30 min. gave 2 : 6-*dimethyloctane-3-thiol*, b. p. 88—89°/10 mm., n_D^{20} 1·4584 (13·2 g., 89%) (Found: C, 69·0; H, 12·7; S, 18·4; thiol-S, 18·4%).

[28] *Org. Synth.*, 1941, **21**, 36.
[29] Norman, LeSuer, and Mastin, *J. Amer. Chem. Soc.*, 1952, **74**, 161.
[30] Djerassi, Gorman, Markley, and Oldenburg, *J. Amer. Chem. Soc.*, 1955, **77**, 568.

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The synthesis of other reference compounds has been described previously.[31]

Thermal Stability of Olefin Sulphuration Products.—Samples of " olefin polysulphides " were heated *in vacuo* at 140° for 5 hr. Elementary and spectroscopic analysis of the products revealed the changes in molecular constitution and complexity as tabulated.

No.	Polysulphide from	Original composition	No.	Composition after heating
1	Oct-1-ene	$(C_8H_{15\cdot6}S_{2\cdot28})_{2\cdot25}$	1*a*	$(C_8H_{16\cdot1}S_{2\cdot16})_{2\cdot62}$
2	2-Methylpent-2-ene	$(C_6H_{12\cdot0}S_{2\cdot16})_{3\cdot06}$	2*a*	$(C_6H_{12\cdot1}S_{2\cdot21})_{2\cdot41}$
3	1-Methyl*cyclo*hexene	$(C_7H_{12\cdot0}S_{2\cdot68})_{2\cdot17}$	3*a*	$(C_7H_{12\cdot1}S_{2\cdot66})_{2\cdot27}$
4	2 : 6-Dimethyloct-2-ene	$(C_{10}H_{20\cdot7}S_{2\cdot6})_{2\cdot18}$	4*a*	$(C_{10}H_{20\cdot6}S_{2\cdot76})_{1\cdot81}$

Polysulphides 1 and 1*a* had similar spectra except for slightly less pronounced absorption at 970 cm.$^{-1}$ in the latter. Samples 2 and 2*a* had similar spectra except for some reduction in trialkylethylenic unsaturation; comparable differences were shown between 3 and 3*a*, and 4 and 4*a*.

We thank Mr. G. M. C. Higgins for the spectroscopic data.

THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION, 48–56 TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, December 23rd*, 1957.]

[31] Moore and Saville, *J.*, 1954, 2089.

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579. *The Reaction of Sulphur and Sulphur Compounds with Olefinic Substances. Part IX.* The Reaction of Sulphur with 2 : 6-Dimethylocta-2 : 6-diene.*

By L. BATEMAN, R. W. GLAZEBROOK, and C. G. MOORE.

Reaction of 2 : 6-dimethylocta-2 : 6-diene (I) with sulphur at 140° yields 2 : 6-dimethylocta-2 : 4 : 6-triene (II), the cyclic monosulphides (III)—(VI), and a cross-linked polysulphide fraction containing two diene (C_{10}) units joined by one or two sulphur cross-links. Increasing the reaction time leads to redistribution of the polysulphidic sulphur in terms of increasing the proportion of cyclic monosulphides and of converting acyclic cross-linked polysulphide into structures having cyclic units based on the skeletal structure of (IV) vicinal to shorter sulphur cross-links.

FARMER and SHIPLEY [1] showed that reaction of sulphur with 2 : 6-dimethylocta-2 : 6-diene (I) at 140° yields a cyclic monosulphide and a cross-linked polysulphide. No detailed investigation of the structures of these cyclic monosulphide or polysulphide products was undertaken, but it was deduced [1] that the former contained 6-ethyl-2 : 2 : 6-trimethylthia*cyclo*hex-3-ene (VIII) and a compound having vinylidene unsaturation, $CH_2{:}CRR'$, as apparently revealed by the infrared spectrum, and this has formed part of the evidence on which broad mechanistic conclusions have been based.[2]

This reaction has now been re-examined in greater detail; the compositions of the cyclic sulphide and cross-linked polysulphide fractions and their variation with time of reaction have been determined. Results and conclusions differing in important respects from those advanced by the earlier workers have been reached, as reported preliminarily elsewhere.[3]

Constitution of the Cyclic Sulphide Fraction.—This fraction contains 2 : 6-dimethylocta-2 : 4 : 6-triene (II) (*allo*cimene), two saturated cyclic sulphides ($C_{10}H_{20}S$) [2-ethyl-2 : 6 : 6-trimethylthia*cyclo*hexane (III) and 2-ethyl-2-methyl-5-*iso*propylthia*cyclo*pentane

* Part VIII, preceding paper.

[1] Farmer and Shipley, *J.*, 1947, 1519.

[2] Farmer, *J. Soc. Chem. Ind.*, 1947, **66**, 86; Bloomfield and Naylor, Proc. XIth Internat. Congr. Pure Appl. Chem., London, 1947, Vol. II, p. 7; Bloomfield, Proc. 2nd Rubber Tech. Conf., London, 1948, p. 79.

[3] Bateman, Glazebrook, Moore, and Saville, Proc. 3rd Rubber Tech. Conf., London, 1954, p. 298.

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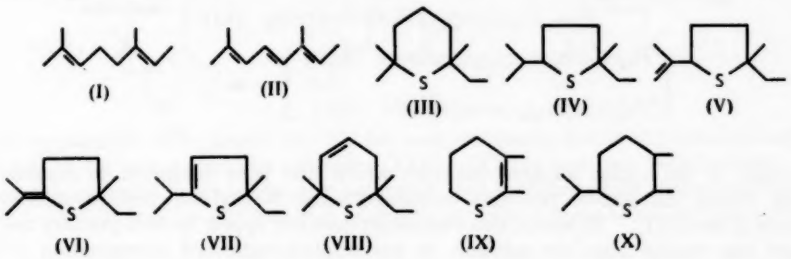
(IV)], and two monounsaturated cyclic sulphides [2-ethyl-2-methyl-5-*iso*propenyl- (V) and 2-ethyl-2-methyl-5-*iso*propylidene-thia*cyclo*pentane (VI)].

The triene (II) and the cyclic sulphides (III)—(VI) were identified mainly by infrared and ultraviolet spectroscopic examination of the bulk cyclic sulphide and of constituent



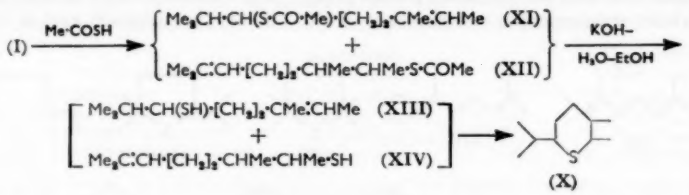
fractions given by a combination of distillation, chromatography, and catalytic hydrogenation.

By a combination of fractional distillation and chromatography on alumina or silica gel, the triene (II) was removed from the cyclic sulphide mixture (which then gave analyses for a mixture of $C_{10}H_{18}S$ and $C_{10}H_{20}S$), and the latter partially resolved into (III)—(VI). The triene (II) was shown by spectroscopy to be predominantly the *trans*-C_4, *cis*-C_6 isomer (cf. O'Connor and Goldblatt [4]) and was estimated by absorption at 2730 Å. The presence of the isomers (III) and (IV) in the cyclic sulphide mixture was established by comparison of the infrared absorption spectrum with those of synthetic (III) and (IV); [5] chromatography gave a fraction which was devoid of (IV), (V), and (VI) and had an infrared spectrum identical with that of pure (III). Although isomers (V) and (VI) have not yet been synthesised (cf. Glazebrook and Saville [5]), evidence for their presence in the mixture can be adduced as follows. Infrared absorption at 1640 and 890 cm.$^{-1}$ in the bulk cyclic sulphide indicated vinylidene unsaturation, $CH_2{:}CRR'$; this is attributed to compound (V) since chromatography on silica gel gave a fraction which was free from (II) and (VI) and contained only minor amounts of (III) and (IV), but had *ca.* 50—60 mole % of $CH_2{:}CRR'$ groups, and on catalytic hydrogenation [6] gave the pure thiophan (IV), as shown by direct comparison with a synthetic specimen. Evidence for the presence of compound (VI) is: (i) selective ultraviolet absorption at 2290—2300 Å, associated with the vinylic sulphide, C:C–S–, chromophore, also shown by the synthetic cyclic sulphide (IX); [7] (ii) removal of ingredients (II), (III), (IV), and (V) by chromatography to give a fraction which had maximum absorption at 2290 Å (ε 7750) but had no infrared absorption attributable to olefinic unsaturation other than the tetrasubstituted type, and on catalytic hydrogenation absorbed hydrogen equivalent to 0·95 double bond per $C_{10}H_{18}S$ molecule to give the cyclic sulphide (IV). The presence of the skeletal structures of (III) and (IV) in the cyclic sulphide fraction was confirmed by conversion of the latter into a cyclic sulphone mixture, $C_{10}H_{18\text{–}20}O_2S$, which on catalytic hydrogenation absorbed hydrogen equivalent to 0·35 double bond per $C_{10}H_{18}O_2S$ molecule to give the sulphones of (III) and (IV).[6]

Contrary to Farmer and Shipley's report,[1] the cyclic sulphide (VIII) could not be detected. None of the cyclic sulphide fractions showed infrared absorption attributable to the *cis*-R·CH:CH·R' grouping, as is observed at 715 cm.$^{-1}$ in the analogous 2 : 2 : 6 : 6-tetramethylthia*cyclo*hex-3-ene.[8] Spectroscopic analysis of all catalytically hydrogenated

[4] O'Connor and Goldblatt, *Analyt. Chem.*, 1954, **26**, 1726.
[5] Glazebrook and Saville, *J.*, 1954, 2094.
[6] Bateman and Shipley, *J.*, 2888.
[7] Bateman and Glazebrook, *J.*, 2834.
[8] Naylor, *J.*, 1949, 2749.

cyclic sulphide fractions also showed the absence of 2 : 3-dimethyl-6-*iso*propylthia*cyclo*hexane (X). For comparative purposes, this compound was synthesised as illustrated:

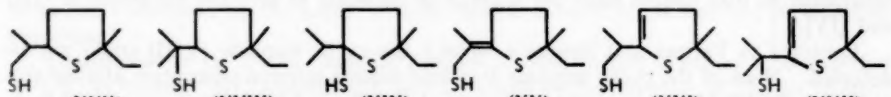


Certain of the cyclic sulphide fractions which had been subjected to considerable heating during distillation probably contained some 5-ethyl-5-methyl-2-*iso*propylthia*cyclo*pent-2-ene (VII). However, this compound does not appear to be a primary reaction product but results from the sulphur- or polysulphide-catalysed isomerisation of (VI) (cf. p. 2850).

Constitution of the Cross-linked Polysulphide Fraction.—The polysulphide mixture obtained from the diene (I)–sulphur reaction at 140° has been less completely analysed, but it has been established that the composition varies considerably with the reaction time and that the cross-linked structures do not, as previously envisaged,[1,2] consist solely of acyclic di-isoprene (C_{10}) units linked as alkenyl alkyl polysulphides but contain cyclic units based on the skeletal structure of (IV) at points vicinal to the polysulphide cross-link. More information about the polysulphide structures follows from fission of the –S–S– bonds with lithium aluminium hydride [5,9] in conjunction with spectroscopic and elementary analyses of the original polysulphide and its hydrogenolysis products.

Analyses of the polysulphide obtained in a 5 hours' reaction indicated a composition $(C_{10}H_{18}S_{2\cdot9})_{1\cdot82}$; the product therefore consists mainly of two di-isoprene units linked by a polysulphide bridge and does not involve repetitive interlinking of diene units by sulphur atoms (cf. refs. 3 and 10). It has much less unsaturation than is required for an alkenyl alkyl polysulphide structure (3 double bonds per C_{20} unit), there being only 0·5—1·0 RR'C:CHR'' group per molecule and smaller amounts (<0·05) of CH_2:CRR'' and possibly *trans*-R·CH:CH·R' groups (<0·1—0·2 per molecule); these findings suggest the presence of cyclic structures. Hydrogenolysis of the polysulphide yielded hydrogen sulphide (indicative of polysulphide cross-links), acyclic monothiol and dithiol, and mercaptocyclic sulphides [$C_{10}H_{18-20}S_2$ (1 SH)], together with a non-cleavable residue (Table 2, expt. 1).

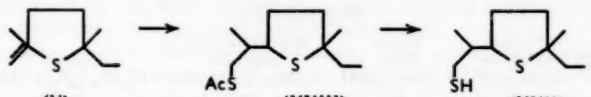
The monothiol proved to be a mixture of a doubly unsaturated compound ($C_{10}H_{17}$·SH) and a monounsaturated compound ($C_{10}H_{19}$·SH), in which the unsaturation is mainly trialkylethylenic with smaller amounts of *trans*-R·CH:CH·R', CH_2:CRR', and C:C·C:C groups, and the thiol grouping mainly tertiary. The infrared spectrum of the dithiol fraction is consistent with the presence of the saturated dithiol (XV) or unsaturated



analogues thereof containing 1 double bond per C_{10} unit, or with a 1 : 2-dithiol such as (XVI), comparable with the 1 : 2-dithiols obtained from hydrogenolyses of polysulphides from mono-olefins.[10] The mercaptocyclic sulphide is largely saturated and appears to

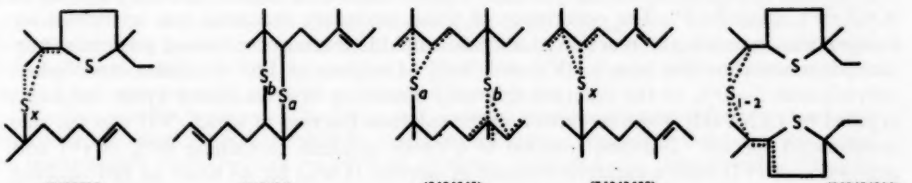
[9] Arnold, Lien, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 731.
[10] Bateman, Glazebrook, Moore, Porter, Ross, and Saville, preceding paper.

consist of the thiophans (XVII) and (XVIII), with possibly (XIX), and minor amounts of their unsaturated analogues (XX), (XXI), and (XXII) containing the C:C–S– chromophore. For reference the mercaptocyclic sulphide (XVII) was prepared by the reaction sequence:



(V) (XXIII) (XVII)

The preparation of the isomer (XVIII) has been previously described,[5] but unambiguous syntheses of the mercaptocyclic sulphides (XIX)—(XXII) have not been realised. The uncleavable material is predominantly saturated, and contains cyclic structures based on (XVII)—(XXII), and smaller amounts of acyclic structures, cross-linked by monosulphide units.



(XXIV) (XXV) (XXVI) (XXVII) (XXVIII)

The above results show that the polysulphide obtained after 5 hours' reaction is composed of both cyclic and acyclic units cross-linked by a mono- or poly-sulphide group as typified by (XXIV)—(XXVII) in which the dotted lines represent the alternative positions of the C–S and C:C bonds.

Analyses of the polysulphide obtained after 50 hours' reaction indicated a composition $(C_{10}H_{17\cdot6}S_{1\cdot46})_{1\cdot74}$, incomplete removal of small amounts of the triene (II) and cyclic sulphides causing the slight departure from a C_{20} unit structure. It consisted essentially of the cross-linked sulphides (XXIV; $x = 1 - 2$) and (XXVIII). Hydrogenolysis yielded only 8% of the total sulphur as hydrogen sulphide, showing that cross-links greater than $-S_2-$ occurred only to a very small extent. The other hydrogenolysis products were mainly uncleavable material (67% of the original polysulphide), containing cyclic sulphide structures based on (XVII)—(XXII) joined by monosulphide cross-links, and mercaptocyclic sulphides [$C_{10}H_{18-20}S_2$ (1-SH)] which consisted mainly of the saturated structures (XVII)—(XVIII), with smaller amounts of (XX)—(XXII).

Influence of Reaction Time on Diene (I)–*Sulphur Reaction.*—Increasing the reaction time from 5 to 50 hours leads to an increased yield of sulphurated product (Table 1) (cf.

TABLE 1. *Reaction of* 2 : 6-*dimethylocta*-2 : 6-*diene* (I) (100 *g.*) *with sulphur* (10 *g.*) *at* 140°.

Expt. no.	Reaction time (hr.)	Cyclic sulphide (*A*) (g.)	Poly-sulphide (*B*) (g.)	Triene (II) (g.)	*A*/*B*	Diene in *A* / Diene in *B*	S (%) in *B*	"Removable sulphur" in *B* *
1	5·0	5·0 †	20·6	0·48	0·42	0·56	40·0	52
2	50·0	12·0 ‡	24·4	0·72	0·85	0·92	25·3	8

* Removed as hydrogen sulphide on hydrogenolysis. † Contains (III) plus (IV), 48%; (V), 41%; (VI), >11%. ‡ Contains (III) plus (IV), 43%; (V), 26%; (VI), 30%; (VII) 1—2%.

Bloomfield [11] and Ross [12]) and a redistribution of the polysulphide sulphur, reflected in the decreased sulphur content of the polysulphide and the increased amount of cyclic sulphide in the total product. The compositions of the products also change markedly; the yield of the cyclic sulphide (VI) increases relatively to that of (V), although changes

[11] Bloomfield, *J. Soc. Chem. Ind.*, 1949, **68**, 66.
[12] Ross, following paper.

in the proportions of the saturated cyclic sulphides (III) and (IV) are slight (Table 1). The two reasons for these changes are: first, the incorporation of the thiophan (V) into

TABLE 2. *Composition of polysulphide hydrogenolysis products (yield: wt. % of polysulphide).*

Reaction time (hr.)	Poly-sulphidic sulphur *	Cyclic sulphide $C_{10}H_{18-20}S$	Mono-thiol $C_{10}H_{17-19}$·SH	Mercaptocyclic sulphide $C_{10}H_{18-20}S_2$(1 SH)	Dithiol $C_{10}H_{18-22}S_2$(2 SH)	Higher-boiling products	Loss
5 †	21	0	30	16	18	12	3
50	2	5 ‡	8	17	1	67	0

* Removable as hydrogen sulphide by hydrogenolysis. † Main fraction. ‡ Impurity in polysulphide.

polysulphide structures by interaction with sulphur and/or decomposing polysulphide (see below); secondly, the sulphur- or polysulphide-catalysed isomerisation of the compound (V) to (VI), analogous to the base-catalysed isomerisation of allylic (C:C·C·S⁻) to vinylic (C·C:C·S⁻) sulphides.[13] The occurrence of these secondary reactions was confirmed by independent experiment; reaction of a cyclic sulphide fraction containing predominantly vinylidene unsaturation [due to (V)] with 10% of sulphur at 140° yielded a cross-linked polysulphide (~40% of the reactant mixture) consisting of cross-linked cyclic sulphides typified by (XXVIII), together with a cyclic sulphide fraction in which (VI) was the sole unsaturated species. Further, reaction of a cyclic sulphide containing 60% of (V) and only 4·5% of (VI) with a catalytic amount of sulphur (1·5%) for 48 hours at 140° yielded a cyclic sulphide containing 37% of (V) and 23% of (VI). No isomerisation of (V) to (VI) occurred when the cyclic sulphide was heated alone *in vacuo* for 48 hours at 140°. These reactions are further discussed in Part XI.

With the cross-linked polysulphide, increasing the reaction time leads to redistribution of the polysulphidic sulphur with a decrease in the cross-link to mainly $-S_1-$ and $-S_2-$ units and with more cyclic sulphide structures incorporated in the polysulphide (Tables 1 and 2). Similar changes were observed on heating the polysulphide, isolated after 5 hours' reaction, at 140° for 7 hours: this gave a small amount of cyclic sulphide, consisting mainly of (III) (~75%) with some (VI) (≤27%) and a polysulphide which was largely saturated and contained an increased proportion of cyclic structures as present in (XXVIII).

EXPERIMENTAL

2 : 6-*Dimethylocta*-2 : 6-*diene* (I).—This was prepared by the reduction of purified geraniol,[14] and had b. p. 56·0°/14 mm., n_D^{20} 1·4520.

Synthesis of Cyclic Sulphides.—Compounds (III) and (IV) were prepared as described by Glazebrook and Saville.[5] The thia*cyclo*pentane (IV) formed a *mercuric chloride complex*, m. p. 115—116° (Found: C, 26·9; H, 4·7; Cl, 15·6, 15·65; Hg, 45·2. $C_{10}H_{20}S,HgCl_2$ requires C, 27·0; H, 4·5; Cl, 16·0; Hg, 45·3%).

2 : 3-*Dimethyl*-6-iso*propylthia*cyclo*hexane* (X). The 1 : 5-diene (I) (55 g.) reacted exothermically with mercaptoacetic acid (15·2 g.) at room temperature; the reaction was completed on the steam-bath (30 min.) and the product then fractionated to give a mixture of mercaptoacetates (XI) and (XII), b. p. 126—128°/10 mm., n_D^{20} 1·4828 (28 g., 66%) (Found: C, 67·0; H, 10·25; S, 15·1. Calc. for $C_{12}H_{22}OS$: C, 67·3; H, 10·3; S, 14·95%). This (28 g.) was refluxed under nitrogen with potassium hydroxide (20 g.) in water (100 ml.) and ethanol (100 ml.) for 15 min., and the cooled solution was diluted with water (500 ml.), acidified with acetic acid, extracted with ether, dried, and fractionated, then having b. p. 92—94°/10 mm., n_D^{20} 1·4800 (17 g., 71%) (Found: C, 69·3; H, 11·4; S, 18·3; thiol-S, 10·2. Calc. for $C_{10}H_{19}$·SH: C, 69·8; H, 11·6; S, 18·6; thiol-S, 18·6%). This product in *cyclo*hexane was cooled in running water and irradiated with ultraviolet light for 2 hr. (until the thiol content fell to zero); fractionation then gave compound (X), b. p. 86—89°/8 mm., n_D^{20} 1·4805 (Found: C, 70·3; H, 11·8;

[13] Tarbell and McCall, *J. Amer. Chem. Soc.*, 1952, **74**, 48; Tarbell and Lovett, *ibid.*, 1956, **78**, 2259.
[14] Chablay, *Ann. Chim.* (*France*), 1917, **8**, 145; Dupont, Dulou, and Desreux, *Bull. Soc. chim. France*, 1939, **6**, 84.

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S, 18·3. Calc. for $C_{10}H_{20}S$: C, 69·8; H, 11·6; S, 18·6%), which had an infrared spectrum similar to that of a specimen prepared by Naylor.[15]

Determination of Thiols.—The thiol in ethanol was titrated against standard aqueous silver nitrate and the end-point determined by the amperometric method.[16] In earlier work the thiol was determined by titration against a standard butanol solution of copper butyl phthalate;[17] such determinations are designated C.B.P. below.

Spectrometric Analyses.—(i) *Cyclic sulphide fractions.* The amounts of triene (II) and the cyclic sulphides (III)—(VII) in these were determined as follows: (*a*) The triene (II) by absorption at 2730 Å in EtOH; $\varepsilon = 42{,}870$ at 2730 Å for pure (II);[4] (*b*) (III) by means of a sharp band of medium intensity at 872 cm.$^{-1}$ characteristic of synthetic (III) (this determination is satisfactory except where large amounts of $CH_2{:}CRR'$ groups, which absorb strongly at 890 cm.$^{-1}$, are present); (*c*) (V) by absorption at 890 cm.$^{-1}$; ε determined for 2-methylnon-1-ene and 2 : 4 : 4-trimethylpent-1-ene under comparable conditions; (*d*) (VI) by absorption at 2290 Å; ε 7750 at 2290 Å in EtOH found for fraction (*A* vii) (Table 4) which is assumed to be pure (VI) [this method is applicable only when (VII) is absent]; (*e*) when (VI) and (VII) are both present approximate estimates were obtained from equations correlating the absorption of pure (VI) and of 2-methyl-5-*iso*propylthia*cyclo*pent-2-ene[7] ($\lambda_{max.}$ 2400 Å; ε 2800 in EtOH) at 2290 and 2400 Å with the experimentally observed absorption of the cyclic sulphide mixture at these wavelengths; (*f*) (IV) was estimated by difference since pure (IV) lacks a distinctive band of sufficient intensity to permit estimation in mixtures.

(ii) *Polysulphide fractions.* The types and amounts of olefinic unsaturation in these were determined as described in Part VIII.[10] Identification of the types of C–S linkages was based on spectroscopic characteristics of relevant synthetic sulphides and polysulphides (Higgins, unpublished data).

Reaction of 2 : 6-*Dimethylocta*-2 : 6-*diene* (I) *with Sulphur.*—(1) *Preliminary investigation.* A mixture of the olefin (466 g.) and sulphur (120 g.) was heated with stirring under nitrogen for 52 hr. at 140°. Fractional distillation then gave (i) unchanged olefin (120 g.), b. p. 55—57°/10 mm., n_D^{20} 1·4490; (ii) a small intermediate fraction (16 g.), b. p. 57—85°/10 mm., n_D^{20} 1·4840; (iii) a cyclic sulphide fraction (150 g.), b. p. 85—95°/10 mm., n_D^{20} 1·4870; and (iv) an undistillable polysulphide residue (300 g.).

Examination of the cyclic sulphide fraction (iii). Refractionation through a glass-helix-packed Fenske column gave three approximately equal fractions: (iii*a*) b. p. 84—90°/10 mm., n_D^{20} 1·4840 (Found: C, 69·25, 68·9; H, 11·2, 11·2; S, 18·2; C : H, 10 : 19·3, 19·4. Calc. for $C_{10}H_{18}S$: C, 70·5; H, 10·65; S, 18·85. Calc. for $C_{10}H_{20}S$: C, 69·8; H, 11·6; S, 18·6%); (iii*b*) b. p. 90—92°/10 mm., n_D^{20} 1·4839 (Found: C, 69·85, 69·85; H, 11·3, 11·55; S, 18·65%; C : H, 10 : 19·3, 19·7); (iii*c*) b. p. 92—94°/10 mm., n_D^{20} 1·4934 (Found: C, 69·4, 69·95; H, 10·3, 10·65; S, 18·65%; C : H, 10 : 17·7, 18·2). Fractions (iii*b* and *c*) were combined, and a portion was dissolved in light petroleum and eluted through alumina under nitrogen; the solvent was removed from the eluate and the products were distilled, to give cyclic sulphide (*A*), b. p. 82—90°/10 mm., n_D^{19} 1·4875 (Found: C, 70·75; H, 11·6; S, 18·3%), containing a little of the solvent. Repetition of the above procedure with a further portion of the combined fractions (iii*b*) and (iii*c*) gave cyclic sulphide (*B*), b. p. 88—90°/10 mm., n_D^{19} 1·4880 (Found: C, 70·3; H, 11·25; S, 18·7%; C : H, 10 : 19·1). Spectroscopic analysis of (*A*) indicated approximately 0·7% of the triene (II), 30% of (III), 4% of (V), 27% of (VI), 14% of (VII) and 24% (by difference) of (IV). The product (*A*) in light petroleum was rechromatographed on alumina and then distilled, to give cyclic sulphide (*A*i), b. p. 83—86°/10 mm., n_D^{20} 1·4867 (Found: C, 69·8; H, 11·1; S, 18·5%; C : H, 10 : 19·0), which on catalytic hydrogenation[6] absorbed 0·35 H_2 per $C_{10}H_{18}S$ unit. Distillation of the reduction product gave: (*A*i*H*), b. p. 82—85°/10 mm., n_D^{20} 1·4791 (Found: C, 69·2; H, 11·45; S, 18·8%; C : H, 10 : 19·7), which contained (III) and (IV) in approximately equal proportions, but not the thia*cyclo*hexane (X); ultraviolet absorption indicated a maximum of 2% (VI) plus (VII). Cyclic sulphide (*B*) absorbed 0·38 H_2 per $C_{10}H_{18}S$ unit and gave the product (*BH*), b. p. 82—85°/10 mm., n_D^{20} 1·4796 (Found: C, 69·85; H, 11·25; S, 18·7%), which was mainly (IV) (90—95%) with a little (III), there being no (X) and only a trace of unsaturated groups revealed by a very weak band at ~1640 cm.$^{-1}$. Treatment of product (*BH*) with mercuric chloride gave the mercurichloride derivative of (IV), m. p. and

[15] Naylor, *J.*, 1947, 1532.
[16] Kolthoff and Harris, *Ind. Eng. Chem. Analyt.*, 1946, **18**, 161.
[17] Turk and Reid, *Ind. Eng. Chem. Analyt.*, 1945, **17**, 713.

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mixed m. p. 117° (Found: C, 27·0; H, 4·6; Hg, 45·4. Calc. for $C_{10}H_{20}S,HgCl_2$: C, 27·0; H, 4·5; Hg, 45·3%). The apparent disparity in the relative amounts of (III) and (IV) present in samples (*AiH*) and (*BH*) suggests the non-identity of their respective precursors and this was in part confirmed when infrared analysis of cyclic sulphide (*B*) revealed 16% of (V) and probably <25% of (III). These results indicate partial separation of the components in combined fractions (iii*b* and *c*) to different extents during chromatography and distillation, confirmed by the distillative and chromatographic separations of the components of cyclic sulphide (*A*) described below.

Distillative fractionation of cyclic sulphide (A). Fractionation of sample (*A*) (20 ml.) through a concentric-tube column gave the fractions listed in Table 3.

TABLE 3. *Compositions of fractions derived from cyclic sulphide* (A).

Fraction no.	B. p./mm.	Vol. (ml.)	n_D (temp.)	Formula	Composition (wt. %) (III)	(IV)	(V)	(VI)	(VII)
(*A*ii)	131—133°/83—84	4	1·4851 (19·5°)	$C_{10}H_{18\cdot6}S$	35	0	0	43	35
(*A*iii)	133—138°/83—84	6	1·4837 (19°)	$C_{10}H_{19\cdot2}S$	72	16 *	0	12	—
(*A*iv)	138—139°/83—84	5	1·4834 (19°)	$C_{10}H_{19\cdot2}S$	55	32 *	6	8	—
(*A*v)	105—110°/10	0·5	1·4951 (22°)	$C_{10}H_{19\cdot4}S$	⩽25	0	8	63	Trace
(*A*vi)	110—115°/10	0·5	1·5010 (21·5°)	$C_{10}H_{18\cdot1}S$	Trace	Trace	7	80	Trace

* By difference.

Chromatographic fractionation of cyclic sulphide (A). A sample in light petroleum was chromatographed on silica gel (100—200 mesh) and eluted with the same solvent. Four approximately equal fractions were obtained which, after removal of solvent, gave the cyclic sulphide fractions whose compositions are given in Table 4. Confirmation that fraction (*A*vii) was substantially pure (VI) was the absorption of 0·95 H_2 per $C_{10}H_{18}S$ unit, to give a cyclic sulphide (*A*vii*H*) consisting of substantially pure (IV) with a maximum of 2% of (VI) and no (III), (V), or (X).

TABLE 4. *Cyclic sulphides* (%) *in fractions derived from cyclic sulphide* (A) *by chromatographic separation.*

Fraction no.	n_D^{20}	(III)	(IV)	(V)	(VI)
(*A*vii)	1·5049	0	0	0	100
(*A*viii)	1·4885	0	50—60	8	40
(*A*ix)	1·4828	35	55	7	6
(*A*x)	1·4822	100	0	0	—

Oxidation of cyclic sulphide (A*i*) *to sulphone.* Cyclic sulphide (*Ai*) (8·8 g.) on oxidation with hydrogen peroxide–acetic acid at 0° gave sulphone (*AiS*), b. p. 92—94°/0·01 mm., n_D^{20} 1·4880 (8·4 g., 80%) (Found: C, 58·95; H, 9·5; S, 15·55; C : H, 10 : 19·2. Calc. for $C_{10}H_{18}O_2S$: C, 59·5; H, 8·9; S, 15·85. Calc. for $C_{10}H_{20}O_2S$: C, 58·9; H, 9·8; S, 15·7%), which absorbed 0·35 H_2 per $C_{10}H_{18}O_2S$ molecule, to give a saturated sulphone (*AiSH*), b. p. 78—79°/0·01 mm., n_D^{20} 1·4836 (Found: C, 58·9; H, 9·8; S, 15·65%; C : H, 10 : 19·8). This consisted of the sulphone derivatives of (III) (47%) and (IV) (53%).

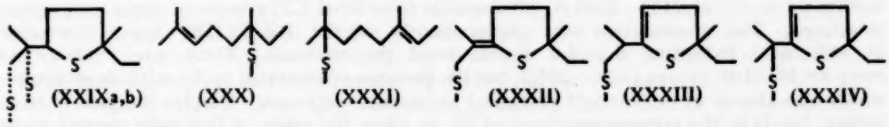
Reaction of 2 : 6-*Dimethylocta*-2 : 6-*diene* (I) *with Sulphur.*—(2) 50 *hours' reaction.* A mixture of the olefin (90·0 g.) and sulphur (9·0 g.) was heated *in vacuo* for 50 hr. at 140°. Fractional distillation then gave unchanged olefin, a cyclic sulphide fraction (*C*), b. p. 88—94°/10 mm., n_D^{20} 1·4950 (20·5 g.) (Found: C, 71·5; H, 11·2; S, 16·9%; C : H, 10 : 18·7), and a polysulphide residue (*D*) (21·9 g.) involatile at 60°/0·001 mm. [Found: C, 64·7; H, 9·55; S, 25·3%; *M*, 313, 327. Corresponds to $(C_{10}H_{17\cdot6}S_{1\cdot46})_{1\cdot74}$]. Fraction (*C*) contained approximately 7% of the triene (II), 24% of (V), 28% of (VI), 1—2% of (VII), and (III) and (IV) in roughly equal proportions.

Hydrogenolysis of polysulphide (D). The polysulphide (*D*) (10·0 g.) in tetrahydrofuran (50 ml.) was added to lithium aluminium hydride (3 g.) in tetrahydrofuran (100 ml.) and the mixture refluxed for 6 hr. The product was decomposed with 2N-sulphuric acid (100 ml.) at 0° and the evolved hydrogen sulphide removed in a current of nitrogen and collected in aqueous lead acetate to give lead sulphide (1·5 g.; *i.e.*, 8% of "removable sulphur"). The hydrogenolysis products were extracted with light petroleum and fractionated, to give: (*Di*), b. p. <55°/0·01 mm., n_D^{20} 1·5073 (1·05 g.) (Found: C, 66·8; H, 10·15; S, 22·1; thiol-S, 11·5%; C : H, 10 : 18·1; *M*, 176, 190); (*Dii*), b. p. 55—57°/0·01 mm., n_D^{20} 1·5189 (0·96 g.) (Found:

C, 64·7; H, 9·9; S, 25·9; thiol-S, 13·7%; C : H, 10 : 18·2; *M*, 183, 196); (*Di*iii), b. p. 57—60°/0·01 mm., n_D^{20} 1·5236 (1·12 g.) [Found: C, 60·5; H, 9·7; S, 29·55; thiol-S, 18·1%; C : H, 10 : 19·1; *M*, 199, 213. Calc. for $C_{10}H_{18}S_2$ (1SH): C, 59·5; H, 8·9; S, 31·7; thiol-S, 15·8%; *M*, 202. Calc. for $C_{10}H_{20}S_2$ (1SH): C, 58·8; H, 9·8; S, 31·4; thiol-S, 15·6%; *M*, 204]; (*Di*v), b. p. <100°/0·001 mm., n_D^{20} 1·5336 (4·16 g.) [Found: C, 67·3; H, 10·05; S, 22·25; thiol-S, 6·75%; C : H, 10 : 17·8; *M*, 287, 300. Corresponds to $(C_{10}H_{17\cdot8}S_{1\cdot24})_{1\cdot66}$]; and (*Dv*) an undistillable residue (*ca.* 2·5 g.), not further examined. The sulphur and thiol contents of the above fractions together with their molecular weights permitted the determination of the amounts of monothiol, dithiol, and mercaptocyclic sulphide formed (Table 2).

A second polysulphide (*Da*) (Found: C, 61·5; H, 9·3; S, 29·2%), comparable to polysulphide (*D*), was obtained by evaporative distillation at <110°/10^{-3} mm. of the polysulphide residue obtained from reaction of (I) with sulphur for 52 hr. at 140° (section 1, p. 2851). Hydrogenolysis of polysulphide (*Da*) (16·0 g.) gave negligible hydrogen sulphide and the following fractions: (*Da*i), b. p. <60°/0·01 mm., n_D^{20} 1·5041 (1·4 g.) [Found: C, 62·3; H, 10·2; S, 27·3; thiol-S (C.B.P. method), 16·2%; C : H, 10 : 19·5; *M* (cryoscopic in C_6H_6), 188]; (*Da*ii), b. p. 60°/0·01 mm., n_D^{20} 1·5160 (2·7 g.) [Found: C, 60·15; H, 9·85; S, 29·95; thiol-S (C.B.P. method), 15·8%; C : H, 10 : 19·5; *M*, 203, 208]; (*Da*iii), b. p. 60°/0·01 mm., n_D^{20} 1·5210 (2·7 g.) [Found: C, 59·9; H, 9·6; S, 30·9; thiol-S (C.B.P. method), 16·4%; C : H, 10 : 19·1; *M*, 202, 203. Calc. for $C_{10}H_{18}S_2$(1 SH): C, 59·35; H, 8·95; S, 31·7; thiol-S, 15·85%; *M*, 202·4. Calc. for $C_{10}H_{20}S_2$ (1SH): C, 58·75; H, 9·9; S, 31·35; thiol-S, 15·7%; *M*, 204·4]; (*Da*iv), b. p. 60°/0·01 mm., n_D^{20} 1·5278 (1·4 g.); and (*Da*v), residue (6·0 g.) which on molecular distillation at 60—105°/10^{-3} mm. gave: (*Da*vi), n_D^{18} 1·5340 [Found: C, 65·4; H, 9·95; S, 24·25; thiol-S (C.B.P. method), 5·6%; *M*, 310. Corresponds to $(C_{10}H_{18\cdot1}S_{1\cdot39})_{1\cdot76}$]; (*Da*vii), n_D^{18} 1·5350 [Found: C, 66·45; H, 10·05; S, 23·2; thiol-S (C.B.P. method), 3·0%; *M*, 322, 328. Corresponds to $(C_{10}H_{18\cdot6}S_{1\cdot31})_{1\cdot81}$]; and (*Da*viii), n_D^{18} 1·5400 [Found: C, 66·6; H, 9·9; S, 23·8: thiol-S (C.B.P. method), 1·9%; *M*, 365. Corresponds to $(C_{10}H_{17\cdot7}S_{1\cdot34})_{2\cdot02}$].

Spectroscopic Examination of Polysulphides (D) *and* (Da) *and Their Hydrogenolysis Products.*—Sample (*D*) showed weak infrared absorption bands attributable to minor contamination with cyclic sulphide and triene (II), which is also indicated by the analyses of the polysulphide and its hydrogenolysis products (*Di*) and (*Di*i), and by ultraviolet absorption thereof at 2300—2350 and 2800 Å, attributed to ~6—10% of (VI) and ≤2% of (II), respectively. The infrared spectrum of (*Da*) resembled that of the mercaptocyclic sulphide (XVIII), suggesting that (*Da*) consists essentially of cyclic sulphide units cross-linked by sulphur atoms, and this accords with the analysis of the hydrogenolysis products (*Da*i)—(*Da*iv). The spectra of the latter resemble that of the tertiary mercaptocyclic sulphide (XVIII) more than that of the primary mercapto-analogue (XVII). The higher-boiling hydrogenolysis fractions (*Da*vi—viii), substantially devoid of thiol groups, are spectroscopically similar to (XVIII); apart from weak infrared absorption attributed to 0·3—0·6 RR′C:CHR″ group per molecule, these samples appear to be saturated. However, they show maximum ultraviolet absorption at 2350—2360 Å attributed to C:C–S groups [(*Da*vi and vii), ~0·45; (*Da*viii), ~0·6]. Similarly, the major hydrogenolysis fraction (*Di*v) of polysulphide (*D*) showed maximum ultraviolet absorption at 2400 Å, indicating ~0·6 C:C–S⁻ group per molecule. It is thus inferred that the fractions (*Da*vi—viii) contain structures (XXIX)—(XXXIV). Since structures (XXXIII) and (XXXIV) contain trisubstituted double bonds and as there is an apparent correlation between the amounts of C:C–S and RR′C:CHR″ groups the observed absorption in (*Da*vi—viii) at ~830 cm.$^{-1}$ may be associated solely with structures (XXXIII) and (XXXIV).



Reaction of 2 : 6-*Dimethylocta*-2 : 6-*diene* (I) *with Sulphur.*—(3) 5 *hours' reaction.* A mixture of the olefin (200 g.) and sulphur (20·0 g.) was heated *in vacuo* for 5 hr. at 140°. The product was cooled at −20° overnight, sulphur (7·0 g.) which had separated was filtered off, and the filtrate fractionated, to give (i) unchanged olefin (168 g.) which contained 2·7% of CH_2:CRR′- and 2·1% of CH_2:CHR-type unsaturation in addition to the original trialkylethylene unsaturation, (ii) a

cyclic sulphide fraction (12·0 g.), collected at 0·1 mm. (bath-temp. at 80—90°) in a trap cooled in acetone–carbon dioxide; and (iii) a polysulphide residue (24·0 g.).

Examination of the cyclic sulphide fraction (ii). Distillation gave a main cyclic sulphide fraction (*E*), b. p. 82—88°/10 mm., n_D^{20} 1·4968 (Found: C, 72·2; H, 10·9; S, 15·65%; C : H, 10 : 18·0) which contained triene (II) 8%, (V) 38%, (VI) ⩾10%, and roughly equal amounts of (III) and (IV); no reliable estimate of (III) was possible owing to the large amount of (V) which masks absorption at 874 cm.$^{-1}$. Cyclic sulphide fractions comparable to (*E*) gave similar analyses: for example, a cyclic sulphide fraction (*F*), b. p. 85—95°/10 mm., n_D^{20} 1·4970 (Found: C, 71·7; H, 10·9; S, 16·45%), contained triene (II) 9·3%, (V) 35—40%, (VI) 15%, and (III) and (IV). Attempts to hydrogenate the cyclic sulphide fraction catalytically failed owing to thiol formation and poisoning of the catalyst (cf. Bateman and Shipley [6]). Fractional elution of cyclic sulphide (*E*) in light petroleum through a silica-gel column gave main fractions: (*E*i), n_D^{20} 1·5300; (*E*ii), n_D^{20} 1·5001; (*E*iii), n_D^{20} 1·4902; (*E*iv), n_D^{20} 1·4908; (*E*v), n_D^{20} 1·4897; (*E*vi), n_D^{20} 1·4897. Fraction (*E*i) contained 73·6% of the *trans*-C_4, *cis*-C_8-triene (II), as indicated by ultraviolet absorption at 2730 Å; identification of other components was not possible because of the large amount of (II) present, but (V) and a small amount of (VI) were probably present. Fraction (*E*ii) contained (II) 12%, (V) ~50%, and (VI) ~20%. Fractions (*E*iii—vi) had similar spectra; (*E*iii) contained 54% of (V) and the other fractions ~50—60% of this compound; the ultraviolet spectra showed a maximum of ~1% of conjugated material [*i.e.*, (II) and (VI)] to be present in these fractions; identification of other compounds was hampered by the large amount of (V) present. Fractions (*E*iii—vi) were combined (1·7 g.) (Found: C, 70·2; H, 11·0; S, 18·2%; C : H, 10 : 18·65); it did not absorb hydrogen catalytically. The cyclic sulphide (1·13 g.) was recovered and a portion (0·85 g.) catalytically hydrogenated; 0·93 H_2 per $C_{10}H_{18}S$ molecule was absorbed, to give a cyclic sulphide (*E*iii—vi*H*), b. p. 80—90°/10 mm., n_D^{20} 1·4728, shown spectroscopically to be almost pure (IV) and confirmed by the formation of the mercurichloride derivative of (IV), m. p. and mixed m. p. 115—116°.

Examination of the polysulphide fraction (iii). A portion (20 g.) in light petroleum was eluted through alumina. After evaporation and removal of a little sulphur, the residue was heated at 60—80°/0·1 mm. for several hours to give a small distillate (Found: C, 59·2; H, 8·75; S, 31·95%; C : H, 10 : 17·6) and a main polysulphide residue (*G*) [Found: C, 51·75; H, 7·8; S, 40·0%; *M*, 414, 428. Corresponds to $(C_{10}H_{18}S_{2\cdot9})_{1\cdot82}$].

Hydrogenolysis of (*G*) (10·0 g.) as above gave hydrogen sulphide (equiv. to 52% of "removable sulphur") and fractions: (*G*i), b. p. <95°/10 mm., n_D^{20} 1·4840 (0·39 g.) (Found: C, 71·75; H, 11·45; S, 16·5; thiol-S, 16·2%; C : H, 10 : 19·0); (*G*ii), b. p. 90—96°/10 mm., n_D^{20} 1·4890 (2·25 g.) (Found: C, 70·1; H, 11·0; S, 18·6; thiol-S, 19·4%; C : H, 10 : 18·7. Calc. for $C_{10}H_{18}S$: C, 70·5; H, 10·65; S, 18·85; thiol-S, 18·8. Calc. for $C_{10}H_{20}S$: C, 69·8; H, 11·6; S, 18·6; thiol-S, 18·6%); (*G*iii), b. p. 56—60°/0·01 mm., n_D^{20} 1·5140 (1·16 g.) (Found: C, 62·2; H, 9·7; S, 27·6; thiol-S, 21·9%; C : H, 10 : 18·6); (*G*iv), b. p. 60°/0·01 mm., n_D^{20} 1·5218 (2·66 g.) (Found: C, 59·35; H, 9·7; S, 30·85; thiol-S, 23·7, 24·0%; C : H, 10 : 19·5; *M*, 224. Calc. for $C_{10}H_{20}S_2$: C, 58·8; H, 9·8; S, 31·4; 1 thiol-S, 15·6; *M*, 204); (*G*v), a residue (1·27 g.) which was evaporatively distilled at 140°/0·01 mm. to give (*G*vi), n_D^{20} 1·5377 (0·61 g.) [Found: C, 64·0; H, 9·75; S, 25·5; thiol-S, 7·8, 8·1%; *M*, 383. Corresponds to $(C_{10}H_{18\cdot2}S_{1\cdot49})_{2\cdot06}$], and (*G*vii), a residue (*ca.* 0·6 g.) [Found: C, 60·3; H, 10·6; S, 27·4; thiol-S, 3·0%. Corresponds to $(C_{10}H_{20\cdot9}S_{1\cdot7})_n$].

Spectroscopic examination of polysulphide (G) *and its hydrogenolysis products.* The infrared spectrum of polysulphide (*G*) indicated that it was more unsaturated than the polysulphides (*D*) and (*Da*), and this was confirmed by comparison of their ultraviolet spectra, *viz.*, higher absorption in (*G*) at 2150—2500 Å, attributable to isolated C:C groups or singly conjugated structures. The unsaturation was predominantly of the RR'C:CHR'' type, absorption at 824 cm.$^{-1}$ indicating 0·5—1·0 double bond per molecule. There was evidence of *trans*-R·CH:CH·R' groups (<10—20%), but the presence of saturated cyclic sulphide structures which also absorb at ~960 cm.$^{-1}$ precluded an accurate estimate. Despite the lack of well-defined bands in the infrared spectrum of (*G*) to allow the types of C–S links present to be definitely identified, it was concluded that the polysulphide had a complex acyclic–cyclic sulphide structure.

The hydrogenolysis fractions (*G*i) and (*G*ii) contained approximately the same amounts and types of unsaturation (RCH:CR'R'', 1·5 per mole; RCH:CHR', 0·1; CH_2:CR'R'', 0·1; C:C·C:C, 0·1). The infrared spectra of both fractions indicated the presence of a saturated

tertiary thio-group, $Me_2C(S^-)R$; weak bands at 1240 cm.$^{-1}$ suggested that small amounts of primary or secondary thiols may also be present. Fractions (*G*iii and iv) were more saturated than (*G*i and ii); they could both contain the mercaptocyclic sulphides (XVII), (XVIII), and (XIX), the intensities of relevant infrared bands indicating a total of ~50% of these structures in agreement with the elementary analytical data. Ultraviolet absorption at 2390—2420 Å in (*G*iv) probably indicates both C:C·C:C and C:C–S$^-$ chromophores, the latter being associated with mercaptocyclic sulphide structures such as (XX), (XXI), and (XXII). The maximum amounts of the above chromophores are 5—5·5% of the former or 19% of the latter. (*G*vi) was similar to (*G*iv) and contained only a small amount of unsaturation which was mainly trialkylethylenic; it contained an appreciable amount of cyclic sulphide structures possessing the skeletal structure of the thia*cyclo*pentane (IV). Sharp-maximum ultraviolet absorption at 2400 Å in (*G*vi) could be due to 0·75 C:C–S$^-$ group or to 0·44 C:C·C:C group per molecule.

Thermal Treatment of Polysulphide.—A sample (5·0 g.) of a polysulphide (*Ga*), similar to (*G*) [Found: C, 51·9; H, 7·95; S, 40·2%; *M*, 407, 413. Corresponds to $(C_{10}H_{18\cdot3}S_{2\cdot9})_{1\cdot77}$], which had been freed from cyclic sulphide by 5 hours' heating at 60°/0·001 mm., was heated *in vacuo* for 7 hr. at 140°, the material becoming darker and more viscous. The product was eluted through alumina with light petroleum, and the eluate fractionated at 90°/0·1 mm., to give cyclic sulphide (*H*) (0·41 g.), n_D^{20} 1·4846 (Found: C, 71·6; H, 11·0; S, 16·8%; C : H, 10 : 18·3), containing (III) ~75%, and (VI) (max. amount 27%); the material also showed very weak maximum absorption at 2820 Å ($E_{1\text{ cm.}}^{1\%}$ 45), which may be due to a small amount of highly conjugated material. The residual polysulphide (*Ia*) (2·64 g.) [Found: C, 52·35; H, 8·55; S, 40·1%; *M*, 430, 431. Corresponds to $(C_{10}H_{19\cdot5}S_{2\cdot87})_{1\cdot86}$] yielded no further distillate from a pot-still at 100°/0·01 mm. in 1 hr. Stripping the alumina column with chloroform gave polysulphide (*Ib*) (1·62 g.) [Found: C, 51·3; H, 7·3; S, 39·9%; *M*, 503, 509. Corresponds to $(C_{10}H_{17}S_{2\cdot9})_{2\cdot2}$]. The infrared spectra of polysulphides (*Ia*) and (*Ib*) were similar and suggested that both samples are nearly saturated, those bands in (*Ga*) assigned to trialkylethylenic groups having practically disappeared; between 1150 and 900 cm.$^{-1}$ the spectra of (*Ia*) and (*Ib*) are similar to those of both mercaptocyclic sulphides (XVII) and (XVIII). Ultraviolet absorption of (*Ib*) at 2150—3000 Å was less than that of (*Ga*), the greatest difference occurring at 2450—2500 Å; this decrease is ascribed to a decrease in content of conjugated structures.

Synthesis of Mercapto-cyclic Sulphide (XVII).—The cyclic sulphide mixture used had n_D^{20} 1·4924 (Found: C, 70·15; H, 11·2; S, 18·6%; C : H, 10 : 19·0). It was free from triene (II) and contained (V) 55%, (VI) >7%, and (III) and (IV) (total ~38% by difference). A mixture of the sulphide (1·8 g.) and redistilled mercaptoacetic acid (5 g.) was irradiated with ultraviolet light in a quartz tube *in vacuo*. Removal of unchanged acid and fractionation gave fractions: (i), b. p. 29—30°/0·01 mm., n_D^{20} 1·4890 (0·31 g.) (Found: C, 68·75; H, 11·35; S, 19·3%; C : H, 10 : 19·7) which contained only (III) (67% based on a band at 874 cm.$^{-1}$) and (IV); (ii), b. p. <103°/0·01 mm. (0·1 g.); and (iii), b. p. 103—105°/0·01 mm., n_D^{20} 1·5207 (1·58 g.), predominantly 5-(2-*acetylthio*-1-*methylethyl*)-2-*ethyl*-2-*methylthia*cyclo*pentane* (XXIII) (Found: C, 58·65; H, 9·0; S, 25·7. $C_{13}H_{22}OS_2$ requires C, 58·5; H, 8·95; S, 26·0%). Hydrolysis of the thiolester (iii) (1·0 g.) with boiling aqueous-ethanolic potassium hydroxide under nitrogen gave 2-*ethyl*-5-(2-*mercapto*-1-*methylethyl*)-2-*methylthia*cyclo*pentane* (XVII), b. p. 65°/0·01 mm., n_D^{20} 1·5214 (0·76 g., 92%) (Found: C, 59·1; H, 9·8; S, 31·3; thiol-S, 17·0, 17·1%; C : H, 10 : 19·8. $C_{10}H_{20}S_2$ requires C, 58·85; H, 9·8; S, 31·35; thiol-S, 15·6%), which gave a red colour with the Rheinboldt test indicating a primary or secondary thiol.

Sulphur-catalysed Thermal Isomerisation of Cyclic Sulphide (V).—The cyclic sulphide had b. p. 98—100°/18 mm., n_D^{20} 1·4895 (Found: C, 70·35; H, 11·0; S, 18·9%; C : H, 10 : 18·7) and contained 60% of (V), 4·5% of (VI), and (IV), but no triene (II). It was unchanged at 140° ± 0·1° *in vacuo* for 48 hr. The sulphide (0·5276 g.) and sulphur (7·8 mg.) were heated *in vacuo* at 140° ± 0·1° for 48 hr. Evaporative distillation *in vacuo* of a portion (0·33 g.) of the product, n_D^{20} 1·4979, gave (i), a cyclic sulphide fraction, n_D^{20} 1·4910 (0·30 g.) (Found: C, 70·5; H, 11·2; S, 18·35, 18·8%; C : H, 10 : 19·0), $\lambda_{max.}$ 2290 Å ($E_{1\text{ cm.}}^{1\%}$ 113) in EtOH, and (ii) a polysulphide residue (0·03 g.) [Found: C, 61·65; H, 9·1; S, 29·15%. Corresponds to $(C_{10}H_{17\cdot6}S_{1\cdot77})_n$]. If the polysulphide (ii) results from the reaction of (V) with sulphur, (VI) and the saturated cyclic sulphides being unaffected, then spectroscopic analysis of (i) indicates 37% of (V) and 23% of (VI); thus of the 0·60 mol. of (V) present in the original cyclic sulphide 0·33 mol. is unaffected, 0·16 mol. is isomerised to (VI), and 0·12 mol. is converted into polysulphide.

Reaction of Diene (I)–*Cyclic Sulphide with Sulphur.*—The cyclic sulphide had n_D^{20} 1·4920

(Found: C, 70·3; H, 10·85; S, 18·3%), $E^{1\%}_{1\,cm.}$ 38 at 2290 Å, and contained 45% of (V), >7% of (VI), and the saturated cyclic sulphides (III) and (IV) [(III > (IV)], but no triene (II). The cyclic sulphide (3·0 g.) and sulphur (0·3 g.) were heated *in vacuo* at 140° for 48 hr. Fractionation of the product gave: (i) cyclic sulphide (1·67 g.), b. p. 90—95°/10 mm., n_D^{20} 1·4937 (Found: C, 70·2; H, 11·2; S, 18·65%), $E^{1\%}_{1\,cm.}$ 268 at 2290 Å in EtOH, containing 59% of (VI) and ~30—40% of (III), but no (V); and (ii) a polysulphide, b. p. <140°/0·01 mm., n_D^{20} 1·5691 (1·3 g.) [Found: C, 57·5; H, 8·85; S, 34·0%; *M*, 385. Corresponds to $(C_{10}H_{18\cdot3}S_{2\cdot2})_{1\cdot84}$]. The polysulphide was predominantly saturated. The presence of cross-linked structures based on the mercaptocyclic sulphides (XVII)—(XIX) is indicated by the infrared spectrum, although this does not resemble (XVII) or (XVIII) sufficiently closely to indicate whether the polysulphide has primary and/or tertiary C–S cross-links. However, the presence of a *gem.*-dimethyl group, indicated by the splitting of the methyl deformation band, shows that some tertiary C–S groups must be present.

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580. *The Reaction of Sulphur and Sulphur Compounds with Olefinic Substances. Part X.*[1] *The Kinetics of the Reaction of Sulphur with* cyclo*Hexene and Other Olefins.*

By G. W. Ross.

The interaction of sulphur and *cyclo*hexene at 110—140° has been studied dilatometrically. The reaction is autocatalytic, and in the early stages the rate is proportional to the square root of the sulphur, olefin, and product concentrations. Other mono-olefins react similarly. 2 : 6-Dimethylocta-2 : 6-diene reacts more slowly than comparable mono-olefins, despite having two double bonds per molecule, and this feature is associated with the formation of cyclic monosulphides in addition to the cross-linked polysulphides similar to those formed from mono-olefins.

The kinetic and product data are consistent with a polar, not a free-radical, chain reaction.

As stated in Part VIII,[2] the kinetic studies now reported are complementary to product studies described in Parts VIII and IX in a programme of work aimed at elucidating the mechanism of sulphur–olefin interaction at about 140°.

Attention has been given mainly to the reaction of sulphur with *cyclo*hexene, because the latter is a relatively good solvent for sulphur, but reactions with 1-methyl*cyclo*hexene, oct-1-ene, hept-2-ene, 2-methylpent-2-ene, 2 : 6-dimethyloct-2-ene, and the 1 : 5-diene, 2 : 6-dimethylocta-2 : 6-diene, have also been examined. The rate of reaction increases until about 20% of the sulphur has reacted and then continues at an almost steady value until nearly all the sulphur is consumed. Further reaction between the product and excess of olefin proceeds at a diminishing rate. Kinetic analysis has been confined mainly to the period of accelerating rate (r_a), and the information obtained appears to justify this procedure rather than considering the steady maximum rate (r_m).

EXPERIMENTAL

Materials.—*cyclo*Hexene was freed from peroxides and purified as described by Bateman and Hughes[3] and stored under nitrogen at −25° until required. The other olefins were as

[1] Part IX, Bateman, Glazebrook, and Moore, preceding paper.
[2] Bateman, Glazebrook, Moore, Porter, Ross, and Saville, *J.*, 1958, 2838.
[3] Bateman and Hughes, *J.*, 1952, 4594.

described in Parts VIII [2] and IX.[1] Immediately before use, the olefin was passed under nitrogen through activated alumina and then distilled under a high vacuum. Sulphur was purified by Bacon and Fanelli's method,[4] and converted into a form suitable for introduction into the dilatometer (capillary tube of 1·5 mm. internal diameter) by grinding and sieving or by recrystallisation from *cyclo*hexane. *cyclo*Hexane was purified by nitration and fractionation (b. p. 80·5°/756 mm.), followed by passage through a column of silica gel. Pure 2 : 2-diphenyl-1-picrylhydrazyl and dibenzyl tetrasulphide were supplied by Lyons and Watson,[5] and Moore, respectively. 1-Azobis-1-phenylpropane was prepared as described by Cohen, Crosvos, and Sparrow.[6] Benzoquinone, trichloroacetic acid, triethylamine, and ethyl sulphide were purified by standard methods; other substances were of " AnalaR " grade and were used directly.

Procedure.—Reaction was followed by observing the volume contraction in a dilatometer with a cathetometer. The dilatometer had a bulb of capacity 4—8 ml. and a capillary tube of 1·5 mm. internal diameter. The olefin was degassed and then distilled at $<10^{-3}$ mm. into the dilatometer containing a weighed quantity of sulphur. Rapid dissolution of the sulphur was effected with vigorous magnetic stirring. Temperature variation during reaction was generally <0·01°; if greater (as over long periods) the volume changes were corrected. Allowance was made for the initial time lag (*ca.* 3 min.) in reaching temperature equilibrium in the thermostat. At the end of a run, the dilatometer was cooled rapidly, the products were transferred to a wide-mouthed tube and degassed, and the unchanged olefin was distilled into a receiver cooled in liquid air and weighed. Unchanged sulphur in the residue was separated by successive filtration and cooling to −25°; the quoted sulphur contents of the polysulphides are probably a little high owing to the solubility of sulphur in these products. Weighings were made at each stage in these operations when it was necessary to correlate volume changes with extent of reaction.

Reaction of cyclo*Hexene with Sulphur.*—(*a*) In a typical experiment, sulphur (0·3048 g.) and olefin (4·0582 g.) were heated at 139·3° for 5 hr.; the contraction in the dilatometer tube was 42 mm. The volatile portion (3·79 g.) of the mixture was unchanged olefin which was analytically (Found: C, 87·6; H, 12·2. Calc. for C_6H_{10}: C, 87·8; H, 12·2%) and spectroscopically pure but contained a trace of thiol (smell and darkening of lead acetate paper). The sulphurated residue (0·56 g.) [Found: C, 39·8; H, 5·5; S, 54·5%; *M* (ebullioscopic in C_6H_6), 367. Calc. for $(C_6H_{10}S_{3.1})_2$: C, 39·7; H, 5·5; S, 54·7%; *M*, 362] did not give a precipitate of sulphur even after one year at −25°. (*b*) Sulphur (2·0 g.), *cyclo*hexene (8·1 g.), and benzene (8·8 g.) were heated *in vacuo* at 150° for 6 hr. with gentle rocking. Evaporation *in vacuo* then gave a fraction of b. p. 79—80° (13·6 g.) and a yellow mobile oil (0·3 g.) (Found: C, 70·1; H, 9·8; S, 19·6%; C : H, 6 : 10). The residue (4·2 g.) (Found: C, 45·1; H, 6·7; S, 48·0; C : H, 6 : 10·6. Calc. for $C_{12}H_{20}S_5$: C, 44·5; H, 6·2; S, 50·8%) contained no phenyl groups as shown spectroscopically.

Results

Until all the sulphur is consumed the sulphurated product can be formulated as two olefin units (RH) linked by several sulphur atoms, *i.e.*, $(RH)_2S_x$ (Table 1). The data are consistent with the product's being a mixture of alkenyl alkyl polysulphide, RS_xRH_2, and a polysulphide with two intermolecular sulphur linkages, ($x = y + z$), as revealed by structural studies.[2] During this period, to which the present kinetic study is restricted, the value of x remains sensibly constant, but it decreases thereafter, while the molecular complexity of the product increases, an effect which reflects the formation of a polymer species, $RS\cdot[S_aRHS_b]_n\cdot SRH_2$, which has also been identified earlier.[2]

Comparable data to those of Table 1 were obtained at 120° and 130°, indicating that the composition of the polysulphide is independent of temperature up to the stage of total combination of sulphur.

Calibration of Volume Contraction.—The linear contraction in the capillary tubing was

[4] Bacon and Fanelli, *Ind. Eng. Chem.*, 1942, **34**, 1043.
[5] Lyons and Watson, *J. Polymer Sci.*, 1955, **18**, 141.
[6] Cohen, Crosvos, and Sparrow, *J. Amer. Chem. Soc.*, 1950, **72**, 3947.

directly proportional to the amount of *cyclo*hexene which reacted, up to 5 hr. at 139·3° (Fig. 1),* as determined by the difference between the original and the recovered amounts of olefin. The amount of sulphur which reacted was deduced from the composition of the polysulphide

TABLE 1. *Composition of* cyclo*hexene polysulphide* (139·3°).

Sulphur concn. (g.-atom/l.)	Time (hr.)	S atoms per *cyclo*hexene unit ($x/2$)	No. of *cyclo*hexene units in polysulphide molecule
1·6	1·5	3·5	2
1·6	2	3·5	2
3·2	2·3	3·7	2
3·2	4	3·4	2
0·8	5	3·2	2
1·6	5	3·1	2
3·2	5	3·1	2
3·2	6 *	2·9	2
1·6	7 *	2·3	2·2
1·6	49 *	0·9	2·5

* Sulphur totally combined.

produced and the amount of olefin which reacted. Since each polysulphide molecule contains two *cyclo*hexene units:

$$[P] = \tfrac{1}{2}[RH]_{changed} = \frac{1}{x}[S]_{changed} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where [P] is the concentration of polysulphide formed in mole/l., and RH and S denote the olefin and sulphur, respectively.

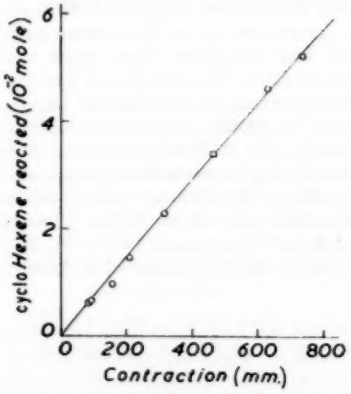


FIG. 1. *Relation between contraction in a* 1·5 *mm. diam. capillary and the amount of* cyclo*hexene reacted.*

A similar relation applies for the other olefins studied.

Kinetic Study of the cyclo*Hexene–Sulphur Reaction at* 139·3°.—A typical run is shown in Fig. 2. During the first 2·5 hr. the rate increases to a maximum which persists for about 2 hr. and then diminishes until after 50 hr. the volume change becomes negligible. For the first 5 hr. the volume change reflects the formation of a polysulphide of approximately constant average composition (Table 1).

For the first tenth of reaction, the following relation was found to hold (Fig. 3 and Table 2):

$$[P]^{\frac{1}{2}} = k(t - t_i)[S]_0^{\frac{1}{2}}[RH]_0^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where t represents total time, t_i an induction period, the suffixes indicate initial concentrations, and k is a proportionality constant. (Variation of $[RH]_0$ was achieved by using *cyclo*hexane as diluent.) The induction periods, t_i, increased with reductions in the sulphur and olefin concentrations and in temperature (*e.g.*, from *ca.* 0·05 hr. at 139·3° to 1·5 hr. at 115° for the

* In certain calibration experiments a dilatometer of 45 ml. capacity with a 4 mm. diameter capillary was used; in Fig. 1 the contraction given is for a 1·5 mm. diameter capillary.

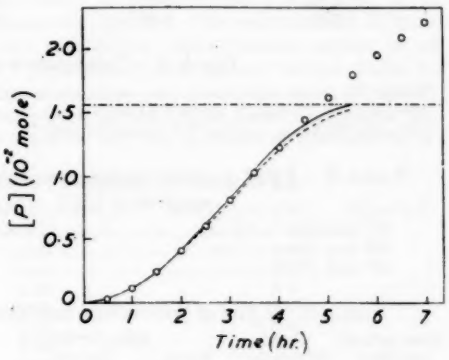
TABLE 2. *Dependence of accelerating rate, r_a, on reactant and product concentrations (139·3°).*

$[S]_0$ (g.-atom/l.)	$[RH]_0$ (mole/l.)	$10^5 r_a[P]^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{-\frac{1}{2}}$ sec.$^{-1}$)	$10^6 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)
0·47	8·43	4·29	2·20
0·71	8·40	5·21	2·14
0·88	2·24	3·19	2·27
0·88	4·65	4·41	2·19
0·88	8·33	5·46	2·02
1·59	8·28	2·44	2·13
1·99	8·22	2·86	2·20
2·26	8·18	3·19	2·34
3·20	8·06	3·44	2·14

concentration conditions of Figs. 2 and 3), but definite correlations with these variables were not established.

FIG. 2. *Course of reaction of sulphur* (2·0 *g.-atom/l.*) *with* cyclo*hexene* (8·2 *mole/l.*) *at* 139·3°.

○ Experimental.
(————) Eqn. 10 ([RH] assumed constant).
(– – – – –) Change in [RH] allowed for.
(— · — · —) Limit of applicability of kinetic scheme.



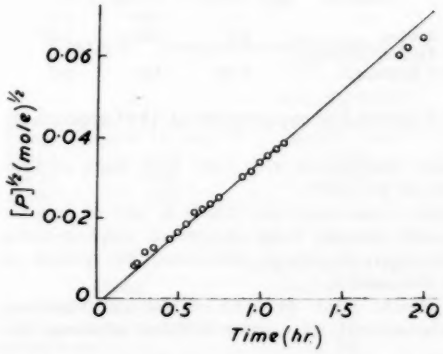


FIG. 3. *Plot of square root of polysulphide formed against time during period of accelerative rate of the sulphur–*cyclo*hexene reaction (reaction conditions as for Fig. 2).*

The rate in this accelerating period, r_a, is then given by:

$$r_a = d[P]/dt = 2k([P][S]_0[RH]_0)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Precise correlation of the maximum rate, r_m, with the reactant variables has not been found possible. However, at the arbitrarily chosen time of half reaction, $t_{\frac{1}{2}}$, when $[S]_{reacted} = [S]_0/2$ then the maximum rate, r_m, is found to be proportional to $[S]_0$ and to the square root of the concentration of olefin then present (Table 3), *i.e.*,

$$r_m = k'[S]_0([RH]_0 - [S]_0 x^{-1})^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Effect of Temperature.—The relations (2), (3), and (4) also hold at 120° and 130°. From results at these temperatures and more limited results at 115° and 125° (Table 4), the Arrhenius

energies of activation for the reactions in the accelerating and the maximum rate regions were the same within experimental error (37 kcal./mole).

Effect of Additives.—"*cyclo*Hexene polysulphide" (Found: C, 54·2; H, 6·3; S, 48·5%) promoted the reaction and gave a constant rate in the early stages which was proportional to the square root of the concentration of the added polysulphide (Table 5).

TABLE 3. *Dependence of maximum rate, r_m, at $t_{\frac{1}{2}}$ on sulphur and* cyclo*hexene concentrations* (139·3°).

$[S]_0$ (g.-atom/l.)	$[RH]_0$ (mole/l.)	$10^5 r_m$ (mole $l.^{-1}$ $sec.^{-1}$)	$10^6 r_m[S]_0^{-1}([RH]_0 - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ $l.^{\frac{1}{2}}$ $sec.^{-1}$)
0·47	8·43	0·67	4·93
0·88	2·24	0·51	4·04
0·88	4·65	0·78	4·18
0·88	8·33	1·25	4·95
1·59	8·28	2·05	4·57
1·99	8·22	2·45	4·39
3·20	8·06	3·34	3·83

TABLE 4. *Temperature dependence of r_a and r_m.*

Temp.	115	120	125	130	139·3
$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ $l.^{\frac{1}{2}}$ $sec.^{-1}$)	0·136	0·216	—	0·725	2·22
$10^6 r_m[S]_0^{-1}([RH]_0 - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ $l.^{\frac{1}{2}}$ $sec.^{-1}$)	0·27	0·43	0·75	1·4	4·5

TABLE 5. *Effect of added* cyclo*hexene polysulphide* (P) *on the* cyclo*hexene–sulphur reaction at* 120°. $[S]_0 = 0·49$ *g.-atom/l.*

[P] (mole/l.)	0·077	0·163	0·236
10^6 rate (mole $l.^{-1}$ $sec.^{-1}$)	1·46	2·07	2·46
10^6 rate $[P]^{-\frac{1}{2}}$	5·25	5·14	5·06

TABLE 6. *Effect of free-radical inhibitors on the sulphur–*cyclo*hexene reaction.*

Free-radical inhibitor	Concn. (10^{-3} mole/l.)	Temp.	$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}$ ($sec.^{-1}$)	Free-radical inhibitor	Concn. (10^{-3} mole/l.)	Temp.	$10^6 r_m[S]_0^{-1}$ ($sec.^{-1}$)
—	—	130°	2·1	—	—	120°	1·22
Quinol	12	130	2·1	Iodine	6·9	120	1·27
Benzoquinone	8·6	130	3·1	Diphenylpicryl-hydrazyl	0·25	120	0·6

Neither 1 : 1'-azo*iso*butyronitrile at 70° nor 1-azobis-1-phenylpropane at 110° appreciably affected the reaction.

Irradiation of the reaction mixture in a silica dilatometer with light from high- or low-pressure mercury lamps failed to induce reaction at 80—100°.

Typical inhibitors and retarders of free-radical chain reactions (Table 6) and of cationic polymerisations (*tert.*-butyl alcohol, pyridine, and dioxan) failed to retard sulphur–olefin reactions. On the contrary, iodine and diphenylpicrylhydrazyl eliminated the period of build-up to maximum rate, while benzoquinone increased r_a.

Trichloroacetic, benzoic, propionic, and stearic acid at 0·05—0·15M-concentrations increased the rate of reaction by 20—50% throughout its course, without affecting the composition of the product.

TABLE 7. *Effect of triethylamine on the sulphur–*cyclo*hexene reaction.*

$[Et_3N]$ (mole $l.^{-1}$)	$[S]_0$ (mole $l.^{-1}$)	Temp.	$10^{-2} r_m[S]_0^{-1}$ (mm. $hr.^{-1}$ mole^{-1} l.)	$[Et_3N]$ (mole $l.^{-1}$)	$[S]_0$ (mole $l.^{-1}$)	Temp.	$10^{-2} r_m[S]_0^{-1}$ (mm. $hr.^{-1}$ mole^{-1} l.)
0	1·65	120°	1·2	0	1·69	135°	7·4
0·33	1·65	120	3·8	0·33	1·69	135	17·0

Triethylamine (0·33 mole $l.^{-1}$) at 120° and 135° decreased the time to reach, and gave a higher, maximum rate (Table 7), in agreement with earlier qualitative observations on amine catalysis of sulphur–olefin reactions.[7] The overall activation energy was reduced from 37 to 31 kcal./mole. During the period when the sulphur is not wholly combined, little change in product composition was detected.

Changing from *cyclo*hexane as diluent to solvents of higher dielectric constant, *viz.*, diethyl sulphide and nitromethane, increased the rate of reaction in this order (Fig. 4), without affecting the sigmoid nature of the extent of reaction–time curve. The product composition was unaffected, and there was no interaction of the sulphur with the solvent.

Although thiols have often been postulated as intermediates,[8,9] only traces have been detected in the products described in Parts VIII [2] and IX.[1] Addition of propane-2-thiol in concentrations from 1 to 50 molar % of the *cyclo*hexene promoted the reaction at 130° without altering the shape of the reaction–time curve (Fig. 5). The increase in rate is not large, however, and does not indicate that the thiol is an active intermediate. Moreover, the volatile material recovered at the end of the reaction always contained unchanged thiol even after 25 hr. at 130°. In the polysulphidic product, *iso*propyl groups were detected spectroscopically and by the C : H ratio, but these could result wholly or in part from the ready exchange reaction between thiols and polysulphides.[10]

Reactions of Sulphur with Other Olefins.—The course of the reactions of sulphur with oct-1-ene, hept-2-ene, 1-methyl*cyclo*hexene, 2-methylpent-2-ene, 2 : 6-dimethyloct-2-ene, and 2 : 6-dimethylocta-2 : 6-diene simulates that with *cyclo*hexene (Fig. 6). The reaction with 2 : 6-dimethyloct-2-ene has been studied in some detail, and kinetic characteristics similar in all respects to those reported above were observed. Equations (3) and (4) are obeyed (Table 8), and the energies of activation associated with the accelerative and maximum rates (38 and 37 kcal./mole, respectively; cf. Table 9) are practically identical with those found for *cyclo*hexene. 1-Azobis-1-phenylpropane had no effect on the reaction, and the free-radical inhibitor tetra-

TABLE 8. *Reaction of sulphur with* 2 : 6-*dimethyloct-2-ene at* 140°.

$[S]_0$ (g.-atom/l.)	$[RH]_0$ (mole/l.)	$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	$10^6 r_m[S]_0^{-1}([RH]_0 - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)
0·49	4·70	3·05	6·9
0·57	0·45	3·05	6·8
0·57	0·92	3·22	6·0
0·57	2·23	3·02	6·6
0·57	3·14	2·94	6·6
0·77	4·68	3·18	7·3
1·10	4·65	3·11	7·3

TABLE 9. *Temperature-dependence of* r_a *and* r_m *for the sulphur–*2 : 6-*dimethyloct-2-ene reaction.*

Temp.	$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	$10^6 r_m[S]_0^{-1}([RH]_0 - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	Temp.	$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	$10^6 r_m[S]_0^{-1}([RH_0] - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)
113·5°	0·11	0·28	130°	1·05	2·16
124·5	0·41	0·89	134·5	2·14	3·54
126·8	0·68	1·31	140	3·08	6·8

TABLE 10. *Reaction of sulphur with olefins at* 140°.

Olefin	$10^5 r_a[P]^{-\frac{1}{2}}[S]_0^{-\frac{1}{2}}[RH]_0^{-\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	$10^6 r_m[S]_0^{-1}([RH]_0 - [S]_0 x^{-1})^{-\frac{1}{2}}$ (mole$^{\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	Composition of polysulphide
Oct-1-ene	1·6	4·1	$[C_8H_{16}S_{2\cdot4}]_{2\cdot2}$ *
2 : 6-Dimethylocta-2 : 6-diene	2·0	4·6	$[C_{10}H_{18}S_{2\cdot1}]_{2\cdot1}$
*cyclo*Hexene	2·3	4·9	$[C_6H_{10}S_{2\cdot1}]_{2\cdot6}$
Hept-2-ene	2·6	6·7	$[C_7H_{14}S_{2\cdot6}]_{2\cdot3}$
2 : 6-Dimethyloct-2-ene	3·1	6·8	$[C_{10}H_{20}S_{2\cdot2_5}]_{2\cdot1}$
2-Methylpent-2-ene	3·9	12·9	$[C_6H_{12}S_{2\cdot2_5}]_{2\cdot2}$
1-Methyl*cyclo*hexene	4·1	6·6	$[C_7H_{12}S_{2\cdot2_5}]_{2\cdot5}$

* For oct-1-ene the reaction time was 11 hr.; for other olefins this was 5 hr.

phenylhydrazine caused no retardation. The polysulphide product catalysed the reaction, as did dibenzyl tetrasulphide at 125°, the square of the rate being a linear function of the polysulphide concentration (Fig. 7).

[7] Moore and Saville, *J.*, 1954, 2082, 2089.
[8] Farmer and Shipley, *J. Polymer Sci.*, 1946, **1**, 293.
[9] Bloomfield and Naylor, Proc. XIth Internat. Congress Pure Appl. Chem., 1947, Vol. II, p. 7.
[10] Birch, Cullum, and Dean, *J. Inst. Petroleum*, 1953, **39**, 206.

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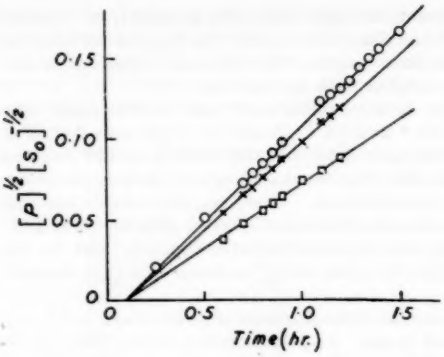
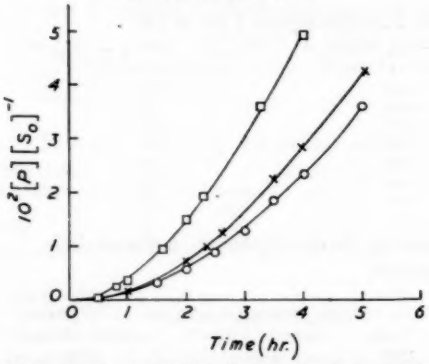


FIG. 4. *Effect of solvent medium on the sulphur–cyclohexene reaction at* 139·3°.

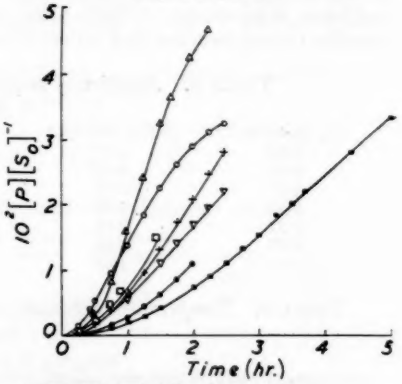
(—□—□—□—) *cyclo*Hexane, ε = 2 at 20°.
(—×—×—×—) Diethyl sulphide, ε = 7·2 at 20°.
(—○—○—○—) Nitromethane, ε = 39·4 at 20°.

FIG. 5. *Effect of propane-2-thiol on sulphur–cyclohexene reaction at* 130°.



Thiol concn. (mole/l.): (—○—○—○—), 0·0. (—×—×—×—), 0·26. (—□—□—□—), 1·34.

FIG. 6. *Course of reaction of sulphur with olefins at* 140°.



(—■—■—■—) Oct-1-ene.
(—×—×—×—) Hept-2-ene.
(—▽—▽—▽—) *cyclo*Hexene.
(—○—○—○—) 1-Methyl*cyclo*hexene.
(—△—△—△—) 2-Methylpent-2-ene.
(—□—□—□—) 2 : 6-Dimethyloct-2-ene.
(—●—●—●—) 2 : 6-Dimethylocta-2 : 6-diene.

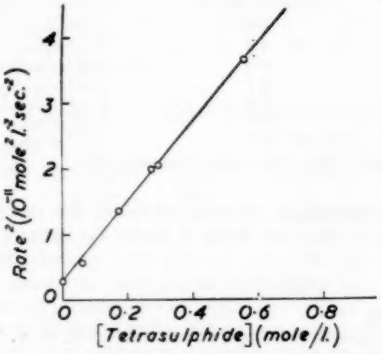


FIG. 7. *Effect of dibenzyl tetrasulphide on rate of reaction of sulphur with* 2 : 6-*dimethyloct-2-ene at* 125°.

Analysis of the rate measurements on the several olefins on the basis of equations (3) and (4) gives the data recorded in Table 10.

Discussion

Olefin–sulphur interaction has been described as a free-radical chain process.[8,9] A polar rather than a free-radical mechanism is now indicated by (*a*) the non-retardation by substances which retard or inhibit known free-radical chain processes; (*b*) the non-catalysis by free-radical initiators and by ultraviolet light; (*c*) the catalysis by polar substances, especially amines and iodine; and (*d*) the increase in reaction rate in solvents of higher dielectric constant. The dependence of the accelerating rate, r_a, on the square root of the sulphur, olefin, and product concentration indicates a chain process in which the termination step involves mutual destruction of two chain carriers.

The annexed *formal* reaction scheme is proposed, which for convenience is restricted to the formation of the alkenyl alkyl polysulphide component of the reaction product.

Chain initiation

$$P \longrightarrow TS_a^+ + TS_b^- \quad \text{R1}$$

Propagation

$$TS_a^+ + RH \longrightarrow TS_aRH^+ \quad \text{Persulphenium ion addition to double bond} \quad \text{R2}$$

$$TS_aRH^+ + RH \begin{cases} \nearrow TS_aR\ (\equiv P) + RH_2^+\ (\equiv T^+) \quad \text{Proton transfer} & \text{R3'} \\ \searrow TS_aRH_2\ (\equiv P) + R^+\ (\equiv T^+) \quad \text{Hydride ion transfer} & \text{R3''} \end{cases}$$

$$T^+ + S_8 \longrightarrow TS_a^+ \quad \text{R4}$$

Termination

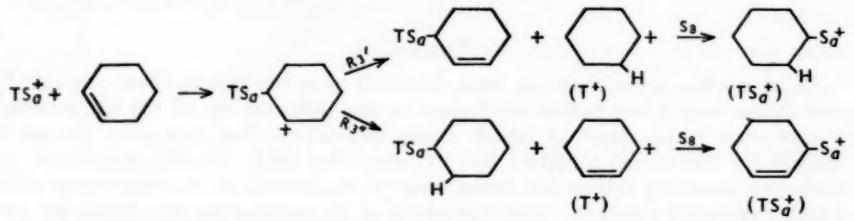
$$\left.\begin{array}{ll} T^+ & + TS_b^- \longrightarrow \\ TS_a^+ & + TS_b^- \longrightarrow \\ TS_aRH^+ & + TS_b^- \longrightarrow \end{array}\right\} \text{Non-chain carriers} \quad \begin{array}{l}\text{R5}\\ \text{R6}\\ \text{R7}\end{array}$$

It will be shown in the following paper that the other main products of mono-olefin sulphuration which have been revealed by the structural studies reported in Part VIII [2] can be explained by rational and kinetically equivalent variants of the propagation steps R2—R4.

Three basic features of the mechanism require comment. First is the heterolysis of an S–S bond as the initiation step, rather than a homolysis as previously supposed.[8,9] This is a novel postulate, but is not at variance with present knowledge of the reactivity of S–S bonds in sulphur and polysulphides.[11] Secondly, the chain carriers are identified with cations, although a kinetically similar mechanism can be based on participation of the persulphenyl anion in the propagation. This choice is based (i) on the known susceptibility of " non-activated " double bonds to electrophilic attack, and their resistance to nucleophilic reagents,[12] and (ii) on the structures of the products. Thirdly, although the intermediates are formulated as ions, it is not imagined that these exist as such in the reaction environment, but rather that highly polarised molecules and ion pairs or aggregates are formed which react with the ionic character specified. All three features are of considerable general interest and justify a fuller discussion which is given in the following paper.

[11] Bateman, Moore, and Porter, following paper.
[12] Dewar, " The Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949, p. 142.

Application of the formal scheme to *cyclo*hexene indicates how a product having an average alkenyl alkyl polysulphide structure is formed:



In this case the kinetically equivalent reactions R3′ and R3″ yield structurally identical products and thus no means is available to determine their relative participation. With olefins having unsymmetrically substituted double bonds, however, structurally distinct polysulphides will result from the occurrence of R3′ and R3″ and thus their relative importance for these olefins can be deduced. The relative rates of reaction among the mono-olefins (Table 10) are consistent with increase in nucleophilic power and facilitation of reaction R2 by increased alkyl substitution at the double bond. The variation in rate is small, however, probably in part owing to some compensating change of reactivity in the other chain carriers (TS_aRH^+ and T^+) and in part because of the much larger contribution of the initiation reaction, R1, to the overall energetics of the reaction.

Kinetic Requirements of the Reaction Mechanism.—By assuming stationary-state conditions and long kinetic chains, the following rate equation is derived:

$$r^2[P][S][RH] = A^{-1}[S]^{-1}x^2[RH] + B^{-1}x + C^{-1}[S][RH]^{-1} \quad . \quad . \quad (5)$$

where

$$r = d[P]/dt = -\tfrac{1}{2}\, d[RH]/dt = -\frac{1}{x}\, d[S]/dt \quad . \quad . \quad . \quad . \quad (6)$$

$$A^{-1} = k_1^{-1}k_4^{-2}k_5 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$B^{-1} = (k_5 + k_6)k_1^{-1}k_2^{-1}k_4^{-1} + (k_5 + k_7)k_1^{-1}k_3^{-1}k_4^{-1} \quad . \quad . \quad . \quad (8)$$

$$C^{-1} = k_1^{-1}(k_2^{-1}k_6 + k_3^{-1}k_7)(k_2^{-1} + k_3^{-1}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

and reactions R3′ and R3″ are treated as a composite reaction R3.

Equation (5) is seen to be equivalent to the experimentally determined rate in the accelerating region (equation 3) provided A^{-1} and C^{-1} are neglected. This condition holds if the reactions involving the hydrocarbon ion T^+ are either very much faster or slower than the reactions involving the other intermediates. The former case is supported indirectly by the fact that benzene does not participate in the reaction (p. 2857). An interesting consequence of the greater reactivity of the T^+ species is apparent experimentally in the 2 : 6-dimethylocta-2 : 6-diene reaction (see below).

During the early stages of the reaction when [RH] is practically constant, integration of equation (5) (terms in A and C being neglected) gives:

$$2x[P] = [S]_0[1 - \cos(B[RH]_0)^{\frac{1}{2}}t] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Expressing $\cos(B[RH]_0)^{\frac{1}{2}}t$ as a power series and ignoring powers of t greater than the second then leads to:

$$[P] = B[S]_0[RH]_0t^2/4x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

which is identical with equation (2) if $2k = (B/x)^{\frac{1}{2}}$.

The theoretical rate in the accelerating period is therefore given by:

$$r_a = (B/x)^{\frac{1}{2}}([P][S]_0[RH]_0)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

By choosing the time in the region of maximum rate where half the sulphur reacts and substituting the appropriate polysulphide and olefin concentrations then obtaining

{*viz.*, $[S]_0/2x$ and $([RH]_0 - [S]_0x^{-1})$, respectively} into equation (5), and again neglecting terms in A and C, gives the theoretical maximum rate at $t_{\frac{1}{2}}$ as:

$$r_m = B^{\frac{1}{2}}[S]_0([RH]_0 - [S_0]x^{-1})^{\frac{1}{2}}/2x \quad . \quad . \quad . \quad . \quad . \quad (13)$$

This is identical with the experimental expression (equation 4), with $k' = B^{\frac{1}{2}}/2x$.

From the found values of k and k', B and x can be separately evaluated, as for *cyclo*hexene in Table 11. On substituting these into equation (10), then the full lines in Figs.

TABLE 11. *Theoretically derived value of B and x for the sulphur–*cyclo*hexene reaction.*

Temp.	115°	120°	130°	139·3°
$10^4B^{\frac{1}{2}}$ (mole$^{-\frac{1}{2}}$ l.$^{\frac{1}{2}}$ sec.$^{-1}$)	0·29	0·55	1·9	5·5
x	6·4	6·4	6·7	6·0

2 and 8 give the course of the reaction. Agreement with the experimental points is good until 90% of the sulphur has reacted and is further improved by correcting for the change in olefin concentration (broken lines). The values of x determined in this way agree well with experiment (cf. Table 1).

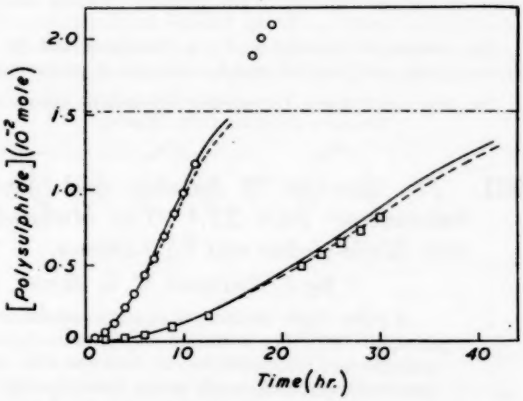


FIG. 8. *Course of reaction of sulphur* (2·0 *g.-atom/l.*) *with* cyclo*hexene at* 120° *and* 130°.

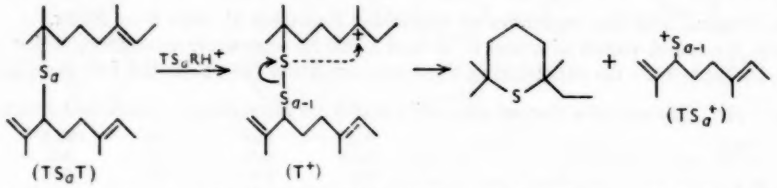
□ Experimental at 120°.
○ Experimental at 130°.
(————) Eqn. 10 ([RH] assumed constant).
(– – – –) Change in [RH] allowed for.
(—·—·—) Limit of applicability of kinetic scheme.

Although equations (5), (12), and (13) have been derived on the assumption of long kinetic chains, this assumption is superfluous if termination occurs solely by reaction R6 (the reverse of the initiation reaction) since rate equations of the same form then result.

The mechanism tacitly assumes that polysulphide is present initially to undergo dissociation to produce a chain carrier, but this is not so. A direct reaction between sulphur and the olefin must therefore precede the chain process, rapidly becoming relatively insignificant as polysulphide is formed. The occurrence of induction periods at the lower temperatures studied and at lower sulphur and olefin concentrations (p. 2858) is consistent with both reactants' engaging in a prior reaction of this kind which proceeds far less readily than the later multistage interaction. The influence of promoters of the overall reaction appears informative in this sense. One class, *e.g.*, acids, do not affect the sigmoid nature of the reaction–time curve and appear to facilitate the propagation reactions, probably by aiding the proton exchange process R3'. Another class, *e.g.*, iodine, amines, and 2 : 2-diphenyl-1-picryhydrazyl, gives an enhanced and initially linear rate of reaction, almost certainly by reacting or forming complexes with the sulphur to give polarised persulphenyl species more readily than does the olefin by direct reaction.[11]

Cyclic Sulphide Formation in the 1 : 5*-Diene System.*—An apparently anomalous feature of the comparative rates of reaction of different olefins (Table 10) is that 2 : 6-dimethylocta-2 : 6-diene reacts more slowly than a strictly comparable mono-olefin (2 : 6-dimethyloct-2-ene) despite having twice the concentration of double bonds as reactive sites. This diene also differs from mono-olefins in yielding a cyclic monosulphide mixture as a major

product.[1] These two features now appear to be related and to reflect a special variant of the reaction mechanism in 1 : 5-diene systems, *viz.*, interaction of an S–S bond of a polysulphide, formed as outlined above, with a carbonium ion formed at an adjacent double



bond by prior proton-transfer with TS_aRH^+, as illustrated. The essential kinetic feature of this process is that the carbonium ion (T^+) is transformed into a cyclic sulphide and the less reactive chain carrier TS_a^+ without consuming elemental sulphur. By thus explaining the reduced rate of reaction, as well as exactly defining the cyclic sulphides formed, strong evidence for the validity of the proposed formal mechanism is provided.

The author is indebted to Dr. L. Bateman and Dr. C. G. Moore for guidance during the course of this work and for much assistance in preparing this paper for publication.

The British Rubber Producers' Research Association, 48–56, Tewin Road, Welwyn Garden City, Herts. [*Received, December 23rd*, 1957.]

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581. *The Reaction of Sulphur and Sulphur Compounds with Olefinic Substances. Part XI.* The Mechanism of Interaction of Sulphur with Mono-olefins and* 1 : 5*-Dienes.*

By L. Bateman, C. G. Moore, and M. Porter.

A polar chain mechanism is advanced for reaction of olefins with sulphur at about 140°; the initiation step is heterolysis of a polysulphide into polar persulphenyl intermediates, at variance with the current view that thermal dissociation of S–S bonds under these conditions occurs homolytically. A review of the literature indicates that, while such homolysis can be induced photochemically or by reaction with other free radicals, it does not occur simply on heating sulphur or organic di- and poly-sulphides at about 140°.

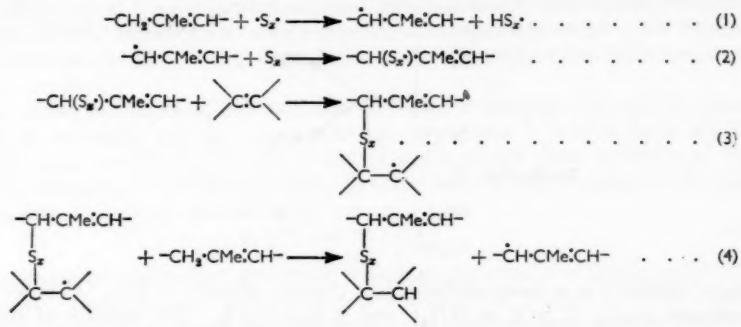
The reaction mechanism, which is consistent with kinetic data (Part X), accounts for the formation of complex polysulphides, including cyclic structures, from oct-1-ene, di- and tri-alkylethylenes and 2 : 6-dimethylocta-2 : 6-diene. The products are complex because a bridged persulphonium intermediate can lose a proton to, or gain a hydride ion from, the olefin (thereby becoming a polysulphide), or combine with sulphur to produce a persulphenium ion which ultimately forms a multi-bridged polysulphide derived from two or more olefin units. These competitive reactions occur in different proportions with different olefins—proton loss is more important than hydride ion gain in an alk-1-ene, while the converse is true for trialkylethylenes.

Cyclic monosulphides formed from the 1 : 5-diene are essentially secondary products resulting from the first formed polysulphides which engage in proton-transfer processes to give sulphurated carbonium ion species: these effect intramolecular heterolysis of adjacent polysulphide linkages, the processes being similar to those postulated for the initial reaction.

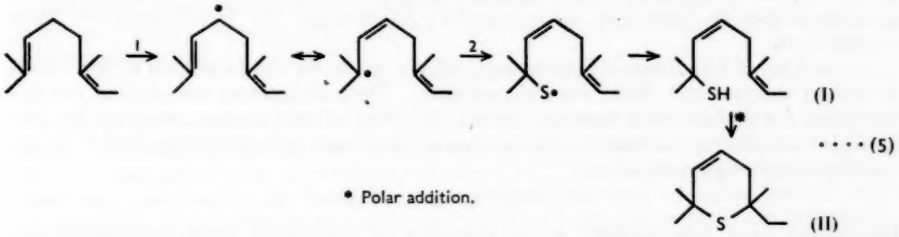
Believing an alkenyl alkyl polysulphide to be the major product of sulphur–mono-olefin interaction at about 140° and the main constituent of the cyclic monosulphide fraction likewise obtained from 2 : 6-dimethylocta-2 : 6-diene to be the thia*cyclo*hex-3-ene (II),

* Part X, preceding paper.

Farmer and his co-workers[1] advanced the following free-radical chain mechanism for olefinic sulphuration:



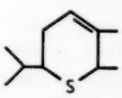
In the special case where the sulphurated radical formed in (2) contains one sulphur atom, alternative reactions to (3) and (4) were proposed, *viz.*, capture of a hydrogen atom, followed by polar or radical addition of the alkenethiol to a second double bond, and this was regarded as the main route to the cyclic monosulphides from 1 : 5-dienes:



* Polar addition.

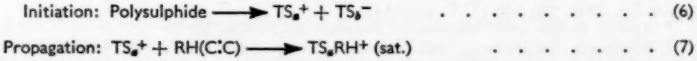
This mechanism has been widely quoted[2] despite little supporting evidence; it was based mainly on an assumed analogy with olefinic autoxidation whose radical-chain nature is well founded.[3]

The detailed structural and kinetic studies reported in the preceding three papers now show: (i) that alkenyl alkyl polysulphides are not the sole primary products of the reaction of mono-olefins with sulphur; (ii) that the alkenyl alkyl polysulphides formed have not the structures to be expected from reactions (1)—(4); (iii) that 2 : 6-dimethylocta-2 : 6-diene does not yield cyclic monosulphides having structures consistent with a wholly free-radical reaction (*e.g.*, III), or with a free-radical reaction yielding a dienethiol (*e.g.*, I) which then undergoes polar intramolecular addition to give (II) as detailed in (5); and (iv) that the kinetic characteristics indicate a polar and not a free-radical mechanism.



(III)

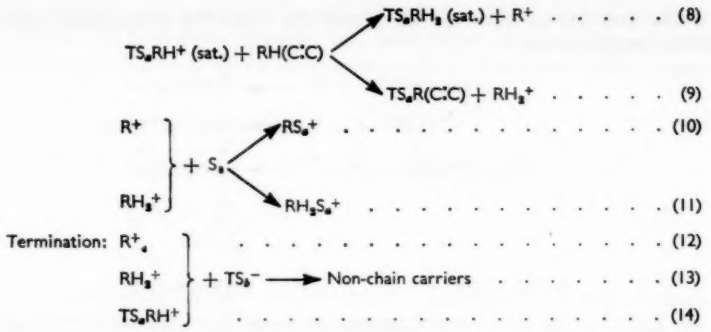
The above mechanism is therefore rejected and a polar mechanism is proposed, which is represented in its simplest form by reactions (6)—(14):



[1] Farmer and Shipley, *J. Polymer Sci.*, 1946, **1**, 293; Farmer and Shipley, *J.*, 1947, 1519; Farmer, *J. Soc. Chem. Ind.*, 1947, **66**, 86; Bloomfield and Naylor, XIth Internat. Congr. Pure Appl. Chem., London, 1947, Vol. II, p. 7.

[2] Flory, "Principles of Polymer Chemistry," Cornell Univ. Press, 1953, p. 454; Burnett, "Mechanism of Polymer Reactions," Interscience Publ. Inc., New York, 1954, p. 89; Grassie, "Chemistry of High Polymer Degradation Processes," Butterworths, London, 1956, p. 246.

[3] Bateman, *Quart. Rev.*, 1954, **8**, 147.



where RH(C:C) is a mono-olefin; (sat.) denotes absence of C:C; H is an α-methylenic hydrogen atom; T is R or RH_2; and a and $b \geqslant 1$. The validity of this mechanism kinetically has been demonstrated by Ross;[4] it will be shown here that reactions (6)—(14) and rational extensions thereof logically account for the major products from mono-olefins or 1 : 5-dienes and sulphur.

The fundamental feature of the proposed mechanism is heterolysis of S–S bonds. Since the reactivity of organic di- and poly-sulphides has often been considered to reflect a susceptibility to homolysis, it is necessary to examine the justification for these suppositions.

Homolysis of S–S *Bonds.*—Convincing evidence exists for the homolysis of S–S bonds in certain thermal and photochemical reactions. Thus, disulphides are efficient radical-acceptors for hydrocarbon radicals formed in vinyl polymerisations initiated by free radicals [5] and during mechanical degradation of elastomers by cold mastication.[6] These reactions may be generalised as:

$$R\cdot + R'S\text{–}SR' \longrightarrow RSR' + R'S\cdot \quad \ldots\ldots\ldots\ldots (15)$$

Disulphides have been shown [7] to be initiators of free-radical vinyl polymerisations, although it is significant that alkyl, aryl, and aralkyl disulphides are effective only under photolytic conditions; photolytic conditions are also essential for disulphides to undergo homolytic thiyl-exchange reactions and for them to initiate the free-radical addition of thiols to olefins.[8] These observations suggest that homolysis of S–S bonds cannot be effected by purely thermal means at temperatures commonly used in reactions of olefins with sulphur (about 140°), but requires either an external free-radical source [*e.g.*, reaction (15) or photochemical activation [9] reaction (16)]:

$$R'S\text{–}SR' \xrightarrow{h\nu} 2R'S\cdot \quad \ldots\ldots\ldots\ldots (16)$$

Kharasch *et al.*[7] and Lecher [10] regard as inconclusive or incorrect earlier evidence cited in favour of thermal homolysis of S–S bonds, such as, *e.g.*, the thermochromic behaviour of disulphides and their non-obeyance of Beer's law,[11] and the reaction of disulphides with

[4] Ross, preceding paper.
[5] Pierson, Costanza, and Weinstein, *J. Polymer Sci.*, 1955, **17**, 221; Costanza, Coleman, Pierson, Marvel, and King, *ibid.*, p. 319, and references therein; Dinaburg and Vansheidt, *J. Gen. Chem.* (*U.S.S.R.*), 1954, **24**, 839 (U.S. transl.).
[6] Ayrey, Moore, and Watson, *J. Polymer Sci.*, 1956, **19**, 1.
[7] Kharasch, Nudenberg, and Meltzer, *J. Org. Chem.*, 1953, **18**, 1233; Birch, Cullum, and Dean, *J. Inst. Petroleum*, 1953, **39**, 206; Ferington and Tobolsky, *J. Amer. Chem. Soc.*, 1955, **77**, 4510; Kern, *ibid.*, p. 1382; Otsu, *J. Polymer Sci.*, 1956, **21**, 559.
[8] Rueggeberg, Cook, and Reid, *J. Org. Chem.*, 1948, **13**, 110; Rueggeberg, Chernack, Rose, and Reid, *J. Amer. Chem. Soc.*, 1948, **70**, 2292; cf. Kharasch *et al.*, ref. 7.
[9] Lyons, *Nature*, 1948, **162**, 1004.
[10] Lecher, *Science*, 1954, **120**, 220.
[11] Schönberg, Rupp, and Gumlich, *Ber.*, 1933, **66**, 1932; Schönberg and Rupp, *Naturwiss.*, 1933, **21**, 561; Koch, *J.*, 1949, 394, 401.

hexaphenylethane in solution to give a monosulphide.[12] Stronger physicochemical evidence is that hot solutions of di(benzothiazol-2-yl) disulphide in toluene are paramagnetic,[13] but Cutforth and Selwood [13] have pointed out that even this is not critical since excitation of the disulphide to a triplet state would produce a comparable effect. No evidence is available [14] that simple alkyl or aryl disulphides display paramagnetism at temperatures up to 140°.

Discussion of the homolysis of S–S bonds in the sulphur molecule, S_8, and in organic polysulphides is especially relevant. Gee and his co-workers [14,15] have described the increase in molecular complexity of liquid sulphur which occurs quite abruptly at 159° in terms of the formation of a linear polymeric diradical form of sulphur which is in equilibrium with S_8 rings:

$$S_8 + \cdot S_x \cdot \rightleftharpoons \cdot S_{x+} \cdot \quad \ldots \ldots \ldots \quad (17)$$

for which confirmation is provided by recent paramagnetic studies of liquid sulphur at 189° and above.[16] However, the existence of diradical forms of sulphur at $\geqslant$159° cannot be offered as evidence that a significant concentration of such species is present in olefinic solutions at ~140°, as required by the free-radical chain mechanism of Farmer *et al.*[1] Sulphur and organic polysulphides are as reactive as disulphides towards hydrocarbon radicals, *e.g.*, alkyl and alkenyl radicals derived from alkyl- or alkenyl-phenyltriazens.[17] By contrast with disulphides, sulphur inhibits the free-radical polymerisation of vinylic monomers,[18] this being ascribed to homolysis of the S–S bond in the S_8 molecule by the polymeric radical [reaction (18)], giving a persulphenyl radical incapable of re-initiating polymerisation:

$$R_n \cdot + S_8 \longrightarrow R_n S_x \cdot \quad \ldots \ldots \ldots \quad (18)$$

Organic polysulphides, $R'S_xR'$ ($x > 2$), also act as polymerisation inhibitors [7] and do not initiate vinyl polymerisation even under photolytic conditions.* No explanation appears to have been offered for the reduced reactivity of $R'S_x \cdot$ ($x \geqslant 2$) compared with $R'S \cdot$ in initiating vinyl polymerisation, but one is probably revealed by recent work [15] which suggests that $R'S_x \cdot$ radicals are partly stabilised by a resonance structure containing a "three-electron bond": $R\text{–}\dot{S}\text{–}S\text{–}S \cdot \longleftrightarrow R\text{–}S\text{–}\dot{S}\cdots S$. Gee *et al.*[15] consider this stabilisation to be responsible for the heat of scission of the S–S bond in a polymeric diradical sulphur chain being <35 kcal./mole, compared with a heat of atomisation of about 428 kcal./mole for the S_8 ring (equivalent to a heat of scission of 53 kcal. per S–S bond in the ring), and point out that in organic polysulphides it will lead to an S–S bond stability sequence in $R'\text{–}\overset{a}{S}\text{–}\overset{b}{S}\text{–}S\text{–}S\text{–}R'$ of $a > b$, if interactions involving the group R′ are neglected.

To summarise: purely thermal homolysis of S–S bonds in sulphur and organic di- and poly-sulphide molecules at temperatures below 140° has not yet been conclusively demonstrated; such fission occurs only when induced photolytically or by a radical displacement reaction such as (15) and (18).

Heterolysis of S–S *Bonds.*—The S–S bonds in sulphur and organic polysulphides are readily broken by nucleophilic reagents, as represented by (19):

$$X^- + \text{–S–S–S–} \longrightarrow \text{–S–S–X} + \text{–S}^- \quad \ldots \ldots \ldots \quad (19)$$

* Birch *et al.*[7] state that di-*tert.*-butyl trisulphide is an exception in this respect, since it photolytically initiates polymerisation of acrylonitrile.

[12] Lecher, *Ber.*, 1920, **53**, 577.
[13] Cutforth and Selwood, *J. Amer. Chem. Soc.*, 1948, **70**, 278.
[14] See Gee, *Trans. Faraday Soc.*, 1952, **48**, 515.
[15] Fairbrother, Gee, and Merrall, *J. Polymer Sci.*, 1955, **16**, 459; Gee, *Sci. Progr.*, 1955, **43**, 193.
[16] Gardner and Fraenkel, *J. Amer. Chem. Soc.*, 1954, **76**, 5891; 1956, **78**, 3279.
[17] Tinyakova, Dolgoplosk, and Tikhomolova, *J. Gen. Chem.* (*U.S.S.R.*), 1955, **25**, 1333 (U.S. transl.).
[18] Bartlett and Trifan, *J. Polymer Sci.*, 1956, **20**, 457 and references therein; Kice, *J. Amer. Chem. Soc.*, 1954, **76**, 6274; *J. Polymer Sci.*, 1956, **19**, 123.

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Common examples include the attack of SO_3^{2-}, CN^-, RS^-, or HS^- ions on sulphur and di- and poly-sulphides [19] and reactions with Grignard reagents (RMgX) and lithium aluminium hydride [20] are probably other examples, the respective nucleophilic species being R^- and AlH_4^-. More recently, evidence has been offered that the non-ionic nucleophiles R_3N: and R_3P: participate in S_N2 reactions at S–S bonds. Jennen and Hens [21] and Krebs [22] formulate the reaction of molecular sulphur with tertiary amines as:

$$R_3N: + S_8 \longrightarrow R_3N^+-S-S_6-S^- \quad \ldots\ldots\ldots (20)$$

and Bartlett and Meguerian [23] obtained kinetic evidence that the reaction of sulphur with triphenylphosphine, to give triphenylphosphine sulphide, involves an initial rate-determining S_N2 heterolysis of S_8 [reaction (21)], followed by a rapid sequence of comparable reactions typified by (22):

$$R_3P: + S_8 \longrightarrow R_3P^+-S-S_6-S^- \quad \ldots\ldots\ldots (21)$$

$$R_3P^+-S-S-S_5S^- \longrightarrow R_3PS + R_3P^+-S-S_5-S^- \quad \ldots\ldots\ldots (22)$$

The reaction of triphenylphosphine with diallyl disulphide has also been interpreted [24] as a polar process [reaction (23)], contrary to the free-radical postulate of Schönberg *et al.*[11,25]:

$$RS-SR \longrightarrow RS^+ + RS^- \xrightarrow{Ph_3P:} [Ph_3P-SR]^+\bar{S}R \longrightarrow Ph_3PS + RSR \quad \ldots\ldots (23)$$

and a similar view is taken of the reaction of triethyl phosphite with diethyl disulphide: [26]

$$(EtO)_3P: + EtS-SEt \longrightarrow [EtS\cdot P^+(OEt)_3]S^-Et \longrightarrow EtS\cdot P{:}O(OEt)_2 + EtSEt \quad \ldots (24)$$

The relevance of reactions (20) and (21) to the function of vulcanisation accelerators and zinc salts in increasing the rate of sulphur–olefin reactions will be discussed elsewhere.

Electrophilic fission of S–S bonds, as is now envisaged in olefin sulphuration, is less well authenticated. One example is thought to be the acid-catalysed interaction of alkyl disulphides with olefins to give bismonosulphides, as in the chain sequence (25)—(28): [27]

$$RS-SR + H^+ \longrightarrow {}^{H}[RS-SR]^+ \quad \ldots\ldots\ldots (25)$$

$${}^{H}[RS-SR]^+ + CH_2=CH_2 \longrightarrow RS-CH_2-CH_2^+ + RSH \quad \ldots\ldots (26)$$

$$RS-CH_2-CH_2^+ + RS-SR \longrightarrow RS-CH_2-CH_2-SR + RS^+ \quad \ldots\ldots (27)$$

$$RS^+ + CH_2=CH_2 \longrightarrow RS-CH_2-CH_2^+ \quad \ldots\ldots\ldots (28)$$

To explain the formation of monosulphides as minor products when *strong* acids such as hydrofluoric acid are used, reactions (29)—(31) are then postulated as an additional chain-initiation process:

$$CH_2=CH_2 + H^+ \longrightarrow CH_3-CH_2^+ \quad \ldots\ldots\ldots (29)$$

$$CH_3-CH_2^+ + RS-SR \longrightarrow {}^{R}[RS-S-CH_2\cdot CH_3]^+ \quad \ldots\ldots\ldots (30)$$

$${}^{R}[RS-S-CH_2\cdot CH_3]^+ \longrightarrow RS\cdot CH_2\cdot CH_3 + RS^+ \quad \ldots\ldots\ldots (31)$$

[19] Foss, *Acta Chem. Scand.*, 1950, **4**, 404; Bertozzi, Davis, and Fettes, *J. Polymer Sci.*, 1956, **19**, 17.
[20] Arnold, Lien, and Alm, *J. Amer. Chem. Soc.*, 1950, **72**, 731; Bordwell and McKellin, *ibid.*, 1951, **73**, 2251.
[21] Jennen and Hens, *Compt. rend.*, 1956, **242**, 786.
[22] Krebs, *Gummi u. Asbest*, 1955, **8**, 68.
[23] Bartlett and Meguerian, *J. Amer. Chem. Soc.*, 1956, **78**, 3710.
[24] Challenger and Greenwood, *J.*, 1950, 26.
[25] Schönberg, *Ber.*, 1935, **68**, 163.
[26] Jacobsen, Harvey, and Jensen, *J. Amer. Chem. Soc.*, 1955, **77**, 6064.
[27] Lien, McCaulay, and Proell, General Papers, Division of Petroleum Chem., Amer. Chem. Soc., 1952, No. 28, p. 169.

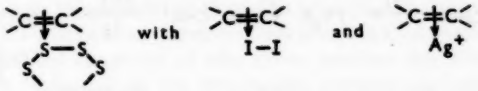
Reactions comparable to (27) and (30)—(31) have been advanced to explain the formation of monosulphides from the thermal reaction of dialkyl disulphides with betaine ($Me_3N^+\cdot CH_2\cdot CO\cdot O^-$) which acts as a source of Me^+ cations [reaction (32)]: [28]

$$RS{-}SR + Me^+ \longrightarrow [RS{-}\overset{Me}{S}R]^+ \longrightarrow RSMe + RS^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (32)$$

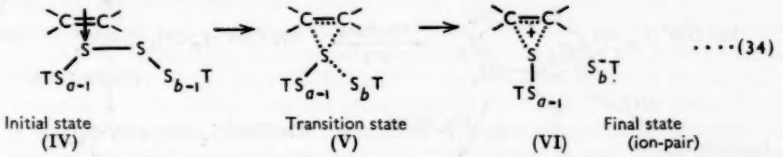
Similarly, the fission of S–S bonds in carboxyl-substituted alkyl disulphides by dimethylformamide (B:) has been formulated as an acid–base-catalysed reaction: [29]

$$B{:}H^+ + RS{-}S{-}CH_2R' \longrightarrow \overset{H}{RS^+}{-}S{-}CH_2R' + B{:} \longrightarrow RSH + {}^+S{-}CH_2R' \xrightarrow{B:} RSH + S{:}CHR' + B{:}H^+ \quad (33)$$

Interaction of S–S *Bonds with Olefinic Double Bonds.*—Reaction (6) has been formally represented as the dissociation of a polysulphide into free persulphenyl ions, which in the prevailing non-polar medium must be associated either as an ion-pair or as constituting a highly polarised molecule. Species of this kind have been postulated in other polar reactions in non-polar solvents where solvation forces cannot provide the large amount of energy necessary for separation (as distinct from formation) of two unlike ions.[30] Polarisation of S–S bonds in sulphur and polysulphide molecules will be promoted by the electron-donor activity of olefinic double bonds, just as this promotes complex formation with iodine,[31] silver ions,[31,32] and various metallic salts,[32,33] cf.:



Such association is essentially similar to, although of a lower order than, the nucleophilic attack of tertiary amines [21,22] and triarylphosphines [23] on sulphur. A truer representation of reactions (6) and (7) is therefore:



The sulphuration process as represented by reaction (34) is thus mechanistically analogous to other reactions involving the addition of electrophilic reagents to olefins in non-polar media, *e.g.*, halogen addition [34] and " allylic " chlorination,[35] ozonolysis,[36] and addition of sulphenyl halides.[37] The cationic moiety of (VI), formulated as a bridged persulphonium ion by analogy with comparable structures [38] and because of certain reactivity characteristics discussed below, appears to be the dominant intermediate in determining the course and products of the overall sulphuration process. The highly complex nature of the products [39] can be related logically to the various possibilities of reaction of this

[28] Challenger, Taylor, and Taylor, *J.*, 1942, 48; Challenger, *Quart. Rev.*, 1955, **9**, 255.
[29] Schöberl and Gräfje, *Naturwiss.*, 1956, **43**, 445.
[30] Hughes, Ingold, Mok, Patai, and Pocker, *J.*, 1957, 1265 and references therein; Ingold, *Proc. Chem. Soc.*, 1957, 279.
[31] Evans, *J. Chem. Phys.*, 1956, **24**, 1244 and references therein.
[32] Chatt, in " Cationic Polymerization," Ed. Plesch, Heffer, Cambridge, 1953, pp. 40 *et seq.*
[33] Douglas, " The Chemistry of the Co-ordination Compounds," Ed. Bailar, Reinhold Publ. Corp., New York, 1956, pp. 487 *et seq.*
[34] de la Mare, *Quart. Rev.*, 1949, **3**, 126.
[35] Taft, *J. Amer. Chem. Soc.*, 1948, **70**, 3364; Salomon, *Proc. Inst. Rubber Ind.*, 1956, **3**, 176.
[36] See Waters, *Ann. Reports*, 1952, **49**, 111.
[37] Hogg and Kharasch, *J. Amer. Chem. Soc.*, 1956, **78**, 2728.
[38] Winstein and Grunwald, *J. Amer. Chem. Soc.*, 1948, **70**, 828; Winstein and Ingraham, *ibid.*, 1952, **74**, 1160.
[39] Bateman, Glazebrook, Moore, Porter, Ross, and Saville, *J.*, 1958, 2838; Bateman, Glazebrook, and Moore, *J.*, 1958, 2846.

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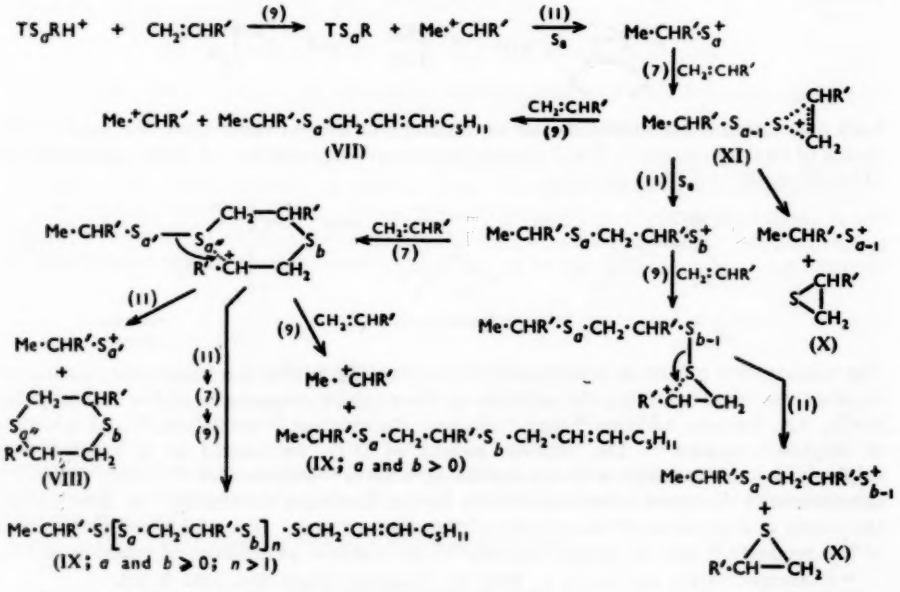
cation, *viz.*, combination with the associated anion or with a sulphur molecule, and proton- or hydride-ion-exchange with an olefin molecule, the differences in product compositions in different olefinic systems reflecting changes in the relative importance of these competing reactions as detailed below.

The persulphenyl anion, TS_b^-, does not appear to participate in the olefinic sulphuration, although it may well facilitate the breaking of the S_8 ring, in keeping with the known ability of sulphenyl anions to induce S–S bond scission,[19] and it will certainly engage in exchange reactions with the polysulphide products.[19] There is no evidence for the addition of this anion to an olefin, this being in accord with the fact that base-catalysed addition of thiols to double bonds occurs only when the latter are activated by electron-attracting substituents (CO_2R, CHO, CN).[40]

Sulphuration of Oct-1-ene.—2-Methylheptyl oct-2-enyl sulphides (VII; $a \geqslant 1$), the cyclic compounds (VIII; a'' and $b \geqslant 1$), and the polymeric material (IX; a and $b \geqslant 0$; $n \geqslant 1$) are major products, and 1 : 2-epithio-octane (X) a minor product, of this reaction.[39] The formation of these compounds (which are not obviously related) and their derivation from common intermediates can be rationalised on the basis of the arguments developed in the last section, as indicated in the annexed reaction scheme, where $R' = C_6H_{13}$ and the numbers refer to reactions already designated.


TS$_a$RH$^+$ + CH$_2$:CHR′ (9) TS$_a$R + Me·$^+$CHR′ (11) S$_8$ Me·CHR′·S$_a^+$
(7) CH$_2$:CHR′
Me·$^+$CHR′ + Me·CHR′·S$_a$·CH$_2$·CH:CH·C$_5$H$_{11}$ (VII) CH$_2$:CHR′ (9)
Me·CHR′·S$_{a-1}$·S: CHR′ CH$_2$ (XI)
(11) S$_8$
Me·CHR′·S$_{a'}$ S$_{a''}$ CH$_2$—CHR′ S$_b$ R′·CH—CH$_2$ CH$_2$:CHR′ (7)
Me·CHR′·S$_a$·CH$_2$·CHR′·S$_b^+$
Me·CHR′·S$_{a-1}^+$ + CHR′ S CH$_2$ (X)
(9) CH$_2$:CHR′
Me·CHR′·S$_a$·CH$_2$·CHR′·S$_{b-1}$
(11)
Me·CHR′·S$_{a'}^+$ + CH$_2$—CHR′ S$_{a''}$ S$_b$ R′·CH—CH$_2$ (VIII)
(11) (7) (9)
(9) CH$_2$:CHR′
Me·$^+$CHR′ +
Me·CHR′·S$_a$·CH$_2$·CHR′·S$_b$·CH$_2$·CH:CH·C$_5$H$_{11}$ (IX; a and $b > 0$)
Me·CHR′·S·[S$_a$·CH$_2$·CHR′·S$_b$]$_n$·S·CH$_2$·CH:CH·C$_5$H$_{11}$ (IX; a and $b \geqslant 0$; $n > 1$)
Me·CHR′·S$_a$·CH$_2$·CHR′·S$_{b-1}^+$ + S R′·CH—CH$_2$ (X)

Important features of this scheme are:

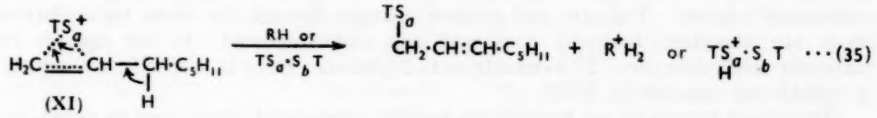
(i) The reactions leading to the different products are the propagation steps in the basic chain mechanism (pp. 2867—8), or kinetically equivalent variants which generate carbonium or persulphenium ionic-type intermediates in the product-forming reactions (to give VIII—X). This justifies kinetic analysis in terms of the basic mechanism, notwithstanding the complexity of the product.[4]

(ii) The bridged persulphonium ion (XI) appears to react mainly (*a*) by combining with sulphur, to give subsequently (VIII), (IX), and (X), and (*b*) by transferring a proton to an olefin, thereby giving (VII). The effect of (*b*) is to cause the sulphur chain in (VII) to

[40] Schöberl and Wagner, "Methoden der Organischen Chemie," Houben-Weyl, Georg Thieme, 1955, Vol. IX, pp. 123 *et seq.*

be attached to the secondary position of the alkyl unit and to the primary position in the alkenyl unit, as is found experimentally.[39]

(iii) The unsaturation pattern in (VII) is that of an allyl sulphide. This strongly suggests that proton elimination occurs in a process specifically involving the bridged persulphonium unit and a β-CH_2 group (reaction 35):

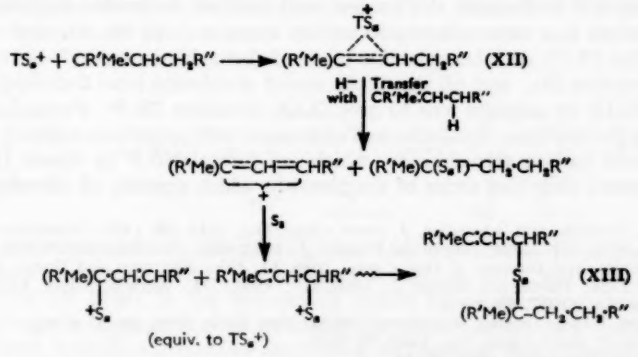


rather than from the carbonium ion $TS_a{-}CH_2{\cdot}\overset{+}{C}H{\cdot}CH_2{\cdot}C_5H_{11}$, which would be expected to give at least a proportion of the more stable vinyl isomer, $TS_a{-}CH{:}CH{\cdot}CH_2{\cdot}C_5H_{11}$.[39,41] This mode of deprotonation and its structural consequences are also evident in the di-isoprenoid system (p. 2877).

(iv) Hydride-ion transfer (reaction 8) appears not to occur to an appreciable extent. Its occurrence would generate the mesomeric cation $\overset{+}{CH_2{=}CH{=}CH}{\cdot}C_5H_{11}$, which should lead to a small but readily detectable amount of the 1-vinylhexyl sulphide structure, $CH_2{:}CH{\cdot}CH(C_5H_{11}){\cdot}S_a{-}$ in the alkenyl unit of the octenyl octyl polysulphide—which is contrary to fact.[39] With other olefins, however, this reaction is of considerable importance.

(v) Neither the detailed structure of any given product nor the different types of product formed can be explained by the free-radical reaction mechanism of Farmer and his co-workers.[1]

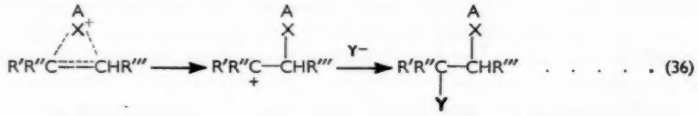
Sulphuration of Di- and Tri-alkylethylenes.—In passing from oct-1-ene to *cyclo*hexene and then to trialkylethylenes the following trends are observed: (i) the rate of sulphuration increases;[4] and (ii) similar products are formed but the proportion of alkenyl alkyl polysulphide increases considerably at the expense of cyclic and polymeric compounds typified by (VIII) and (IX).[39] In the alkenyl alkyl polysulphides obtained from trialkylethylenes, the unsaturation is mainly of the type $CR'R''{:}CHR'''$, and the attachment of the sulphur to the alkyl unit is at the tertiary carbon atom ($-S{-}CR'R''{\cdot}CH_2R'''$),[39] as depicted in (XIII). The second structural feature is compatible with proton-exchange (reaction 9) equivalent to that detailed for oct-1-ene, but the first feature is not, since complete replacement of the original unsaturation pattern by the types $CH_2{:}CR'R''$ and $CHR'{:}CHR''$ (which are found to only a minor extent) would then be required. It appears therefore that in the sulphuration of trialkylethylenes, reaction 9 is of little importance compared with the competitive hydride-ion transfer (8), whose detailed course can be represented as:



[41] Tarbell and McCall, *J. Amer. Chem. Soc.*, 1952, **74**, 48; Tarbell and Lovett, *ibid.*, 1956, **78**, 2259.

Olefins are known to participate in hydride-ion transfers of this type,[42] which will be promoted by alkyl substitution at the far side of the adjacent double bond owing to the greater resonance stabilisation of the resultant allylic carbonium ion (cf. the comparable influence in free-radical olefin autoxidation [3]). Such substitution can thus be expected to facilitate the above sequence of reactions, and in doing so to repress relatively the alternative reactions of the bridged persulphonium ion involving proton-transfer and addition of sulphur. The rate and product changes through the olefin series detailed above are, therefore, mutually consistent and understandable. In the case of the particular trialkylethylene, 2 : 6-dimethylocta-2 : 6-diene, there is a specific consequence of hydride-ion transfer (p. 2877).

One special feature of the hydride-ion transfer represented above may be noted, *viz.*, the attachment of the hydride ion to the least substituted carbon atom of the bridged persulphonium ion (XII), leading to the *tert.*-alkylperthio-linkage in (XIII). The opening of the bridged persulphonium ion (XII) in this way, which in effect is contrary to Markownikoff's rule for polar addition of the electrophile TS_a^+ to a double bond, is unusual but not unique. The usual direction of opening of bridged 'onium ions (XIV; AX = NR_2, SR, or OH, etc.) by attack of a nucleophilic reagent Y^-, recognised in numerous reactions,[38,43] is that leading to (XV), and is attributed[44] to the preferential formation of the tertiary carbonium ion by ring fission of (XIV) before attachment of the addendum Y^-:



(XIV) (XV) . . . . . (36)

The reaction conditions are generally those conducive to this essentially S_N1 type, two-stage process.

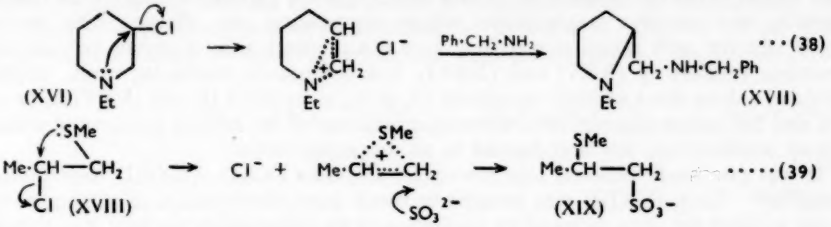
An alternative, S_N2 type process is possible, however, in which ring fission occurs synchronously with nucleophilic attack by Y^- preferentially at the least substituted carbon atom:

. . . . . (37)

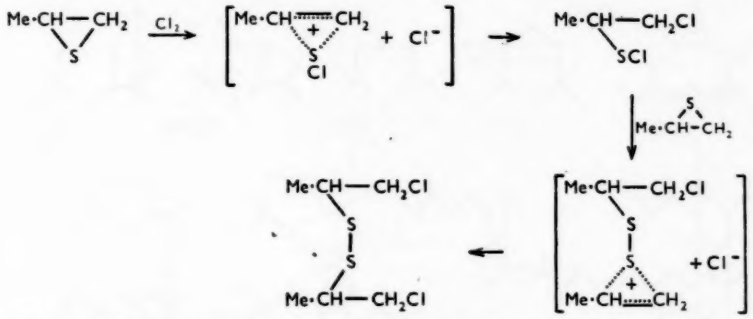
Reactions believed to illustrate this process, and certainly to involve migration of a group (AX) from a less to a more substituted carbon atom, are: (i) the reaction of 3-chloro-1-ethylpiperidine (XVI) with benzylamine to give 2-(benzylaminomethyl)-1-ethylpyrrolidine (XVII) [45] (reaction 38); and (ii) the displacement of chlorine from 2-chloropropyl methyl sulphide (XVIII) by sulphite ions to give (XIX) (reaction 39).[46] Particularly pertinent examples are the reactions of chlorine and of bromine with propylene sulphide in anhydrous chloroform and carbon tetrachloride, which are formulated [47] as shown (for chlorine). It is to be noted that this series of reactions, in which opening of the episulphide ring

[42] Bartlett, Condon, and Schneider, *J. Amer. Chem. Soc.*, 1944, **66**, 1531; Schneider and Kennedy, *ibid.*, 1951, **73**, 5013, 5017, 5024; Moore and Waight, *J.*, 1952, 4237; Baddeley and Pickles, *J.*, 1953, 3726.
[43] Fuson, Price, and Burness, *J. Org. Chem.*, 1946, **11**, 475; Kharasch and Buess, *J. Amer. Chem. Soc.*, 1949, **71**, 2724; Davies and Savige, *J.*, 1950, 317; 1951, 774; Kerwin, Ullyot, Fuson, and Zirkle, *J. Amer. Chem. Soc.*, 1947, **69**, 2961.
[44] Alexander, " Ionic Organic Reactions," Wiley, New York, 1950, pp. 97 *et seq.*
[45] Reitsema, *J. Amer. Chem. Soc.*, 1949, **71**, 2041.
[46] Marvel and Weil, *ibid.*, 1954, **76**, 61.
[47] Stewart and Cordts, *ibid.*, 1952, **74**, 5880.

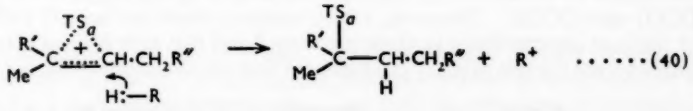
occurs exclusively to give sulphur attachment at the more substituted carbon atom, proceeds in non-solvating media where S_N2 type interaction of the postulated ionic inter-



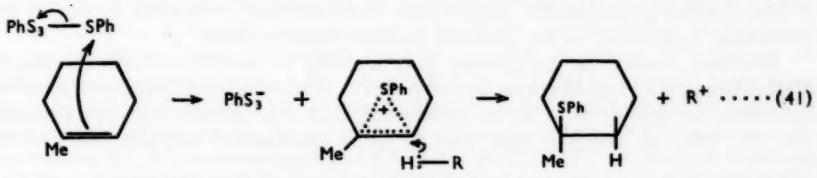
mediate will be favoured, whereas ring-opening in which a bridged sulphonium ion is first converted into a much more labile carbonium ion will not.



The hydride-ion transfer step in the sulphuration process can reasonably be regarded as analogous to the above reactions in being a bimolecular substitution at the least substituted carbon atom of (XII) (reaction 40):



where H–R is the olefin and the hydride ion transferred is α-methylenic. This interpretation of the reaction not only rationalises the present findings but allows apparently anomalous data in the literature to be understood. Thus, Bloomfield [48] found that the main product from the thermal reaction of 1-methyl*cyclo*hexene and diphenyl tetra-



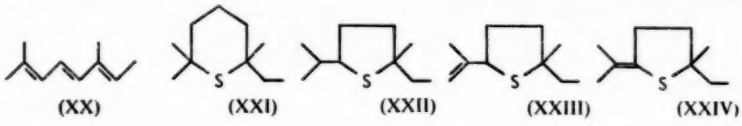
sulphide was 1-methyl*cyclo*hexyl phenyl sulphide, and was unable to account for the addition of the elements of PhSH, or addition in accord with Markownikoff's rule, having regard to the belief in the free-radical nature of sulphuration processes then current.[1] The reaction appears now to be analogous to the reaction of a trialkylethylene with sulphur, with hydride-ion transfer proceeding as specified above (reaction 41).

[48] Bloomfield, *J.*, 1947, 1547.

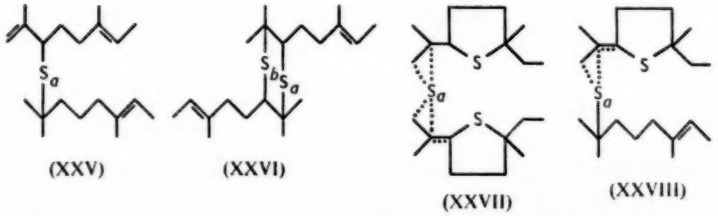
XUM

Sulphuration of 2 : 6-*Dimethylocta*-2 : 6-*diene.*—The products of this reaction are the triene (XX), a cyclic sulphide mixture, consisting mainly of (XXI) and (XXIII), with some (XXII); (XXIV) appears in greater amount at the expense of (XXIII) as reaction proceeds, and complex polysulphides whose composition also changes with reaction time.[39] In the early stages of reaction, there is a predominance of acyclic polysulphidic structures typified by (XXV) and (XXVI), but compounds containing cyclic sulphide units and having short sulphide cross-links (S_1 or S_2) as in (XXVII) and (XXVIII) ($a = 1$ or 2, and the dotted lines represent alternative positions of the sulphur linkage and possible sites of unsaturation) are later formed to an increasing extent.

It was previously believed that the cyclic sulphides (XXI)—(XXIII) were primary products.[49] Thus, (XXIII) was thought to result from direct attack of sulphur at one double bond of the diene followed by cyclisation of an intermediate perthiol (reaction 42). Oxidation of the perthiol to liberate hydrogen sulphide ($2R{\cdot}S_xH \xrightarrow{S} R{\cdot}S_{2x}{\cdot}R + H_2S$) which can then add in a polar manner to the diene to give a mono-olefinic tertiary thiol

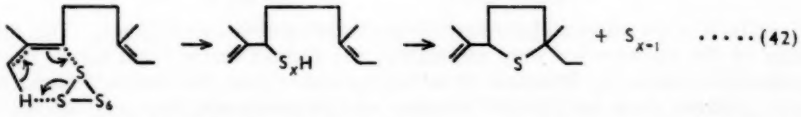


(XX) (XXI) (XXII) (XXIII) (XXIV)



(XXV) (XXVI) (XXVII) (XXVIII)

susceptible to intermolecular addition was held to be the origin of the saturated sulphides (XXI) and (XXII). However, recent evidence does not accord with the participation of thiols as intermediates in these reactions,[4] and it is now believed that the acyclic polysulphides are the sole primary products and that the cyclic sulphides, both free and combined



(42)

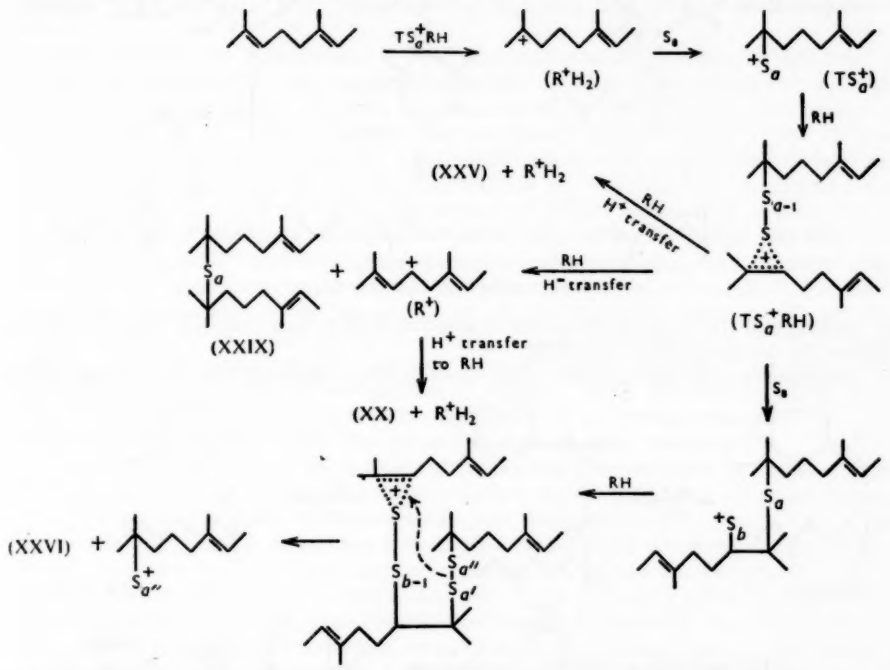
in later formed polysulphides, arise wholly from secondary reactions similar in type and kinetically equivalent to the primary product-forming steps.

Reactions leading to the primary polysulphides in accordance with the sulphuration mechanism now advanced are set out on p. 2877. Only the more important possibilities for isomerism are given; it is to be understood that deprotonation of the persulphonium ion, TS_a^+RH, for example, may lead to some unsaturated sulphide units of the type $\begin{matrix} C \\ C \end{matrix}\!\!>\!C(S_aT){-}C{=}C{-}$ as well as the terminal vinyl type present in (XXV).

Whereas stabilisation of the bridged persulphonium ion, TS_a^+RH, appears to occur predominantly by proton transfer in oct-1-ene and by hydride-ion transfer in singly unsaturated trialkylethylenes, both these processes can be recognised in the di-isoprenic

[49] Bateman, Glazebrook, Moore, and Saville, Proc. 3rd Rubber Techn. Conf., London, 1954, p. 298.

system. Indicative of the first is the formation of vinylic unsaturated units $CH_2{:}CR'R''$ (cf. below), as in the polysulphide (XXV) and the derived cyclic sulphide (XXIII) (see p. 2878), while strong evidence for the second is the formation of the triene (XX). The latter feature further indicates an understandable difference in reactivity of the allylic carbonium ions formed by loss of a hydride ion from the structures $CMe_2{:}CH{\cdot}CH_2R$ and

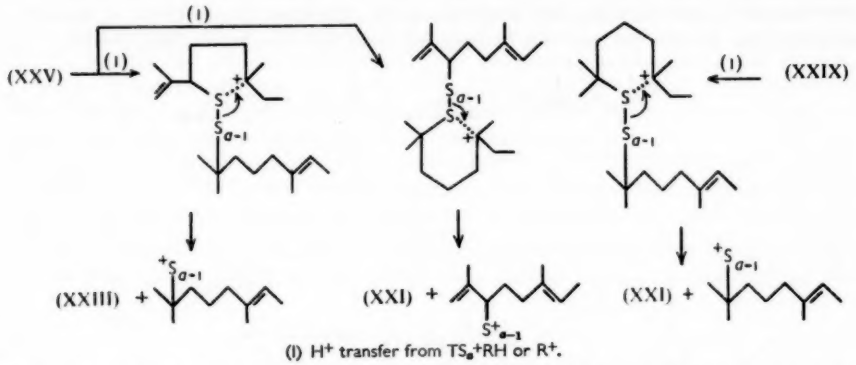


$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CHMe$; in the first case, combination with sulphur ensues to give a persulphenium ion (p. 2873); in the second, the unsaturation pattern provides a strong driving force for a preferential deprotonation, and thus the formation of the highly resonance-stabilised conjugated triene (XX). This triene undoubtedly competes with the diene in the overall sulphuration and is probably the source of the small amount of conjugated diene unsaturation detected in the cross-linked polysulphidic mixture.[39]

The cyclic sulphides (XXI) and (XXIII) can be derived from the primary polysulphides (and also from isomers resulting from initial protonation at the other double bond in the diene) by intramolecular reactions induced by, and involving, active intermediates analogous to those postulated for the primary sequence of reactions as exemplified in the annexed scheme. The allylic sulphide (XXIII) is known [39] to undergo a sulphur-catalysed isomerisation to the vinylic isomer (XXIV), and would be expected to undergo other reactions leading to the saturated thia*cyclo*pentane (XXII) and to polysulphidic-cyclic sulphide structures such as (XXVII) and (XXVIII): analogous reactions applied to cross-linked polysulphides of type (XXVI) lead to similar polysulphidic-cyclic sulphide structures. The formation of (XXVIIb) accords with the finding of conjugated vinylic sulphide units in these structures although they are absent from the acyclic polysulphides.[39]

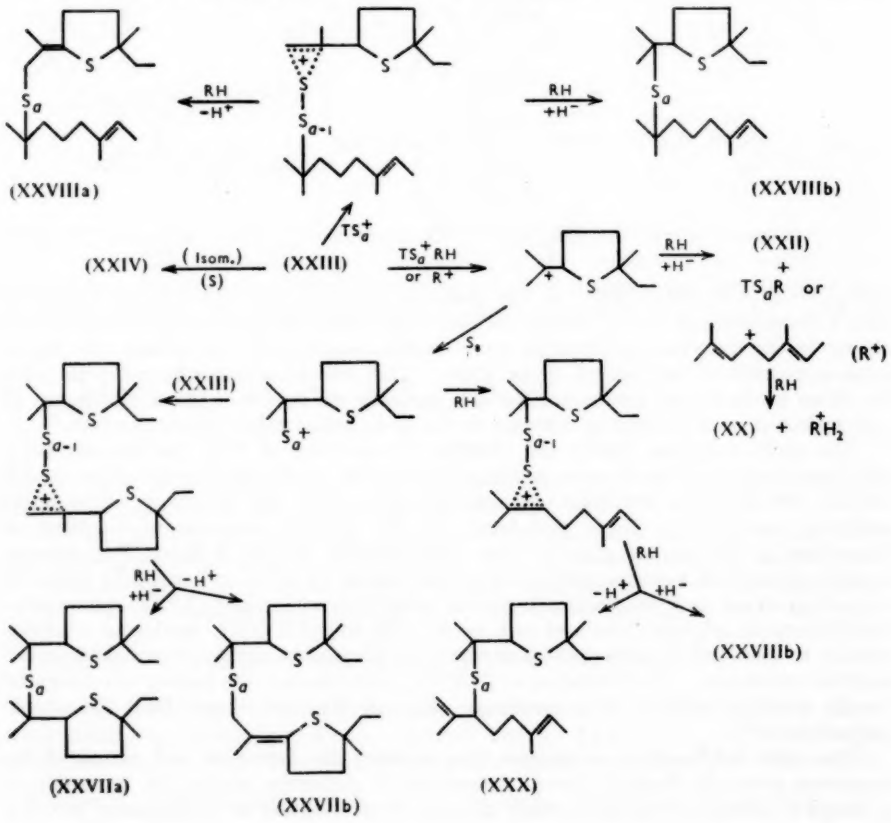
The basic sulphuration mechanism thus explains the formation and nature of the numerous products detailed above. Conversely, it definitely implies the formation of a complex mixture of products which changes in composition as sulphuration proceeds

as a result of successive reactions involving products as well as primary reactants and yet conforming to a single kinetic pattern. One significant kinetic distinction between the



1 : 5-diene and the mono-olefin system is associated with cyclic sulphide formation in the former, as discussed below (p. 2879).

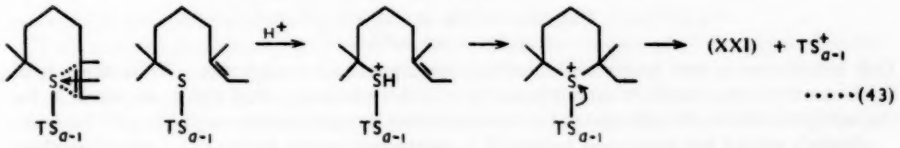
Sulphuration of Polyisoprenes.—The cross-linking (vulcanisation) of natural rubber



by sulphur alone at 140° is a very inefficient reaction; each effective cross-link requires the combination of some 40—60 atoms of sulphur.[49, 50] This has been attributed [51] to the incorporation of the sulphur (*a*) in multi-atom cross-links (S_4—S_8), and (*b*) in cyclic sulphide (non-cross-linking) structures; to these must now be added (*c*) in adjacent cross-links, as in (XXVI), which act physically as a single cross-link. The present work throws light on three aspects of this technologically important and hitherto little understood subject.

First, contrary to earlier ideas, [49, 51] no acceptable mechanism can be advanced to explain the formation of cyclic sulphide independently of, and yet competitive with, the formation of polysulphide. Secondly, although acyclic polysulphides are now held to be the precursors of the cyclic sulphides, this conversion does not result in the ultimate destruction of a cross-link (cf. ref. 51); a persulphenium ion, TS_a^+, is concurrently produced and this forms a new cross-link by reaction with the polyisoprene. The inefficient use of sulphur in this sense is in fact more subtle than previously supposed; [51] it involves, not the destruction of cross-links, but the diversion of carbonium and bridged persulphonium ion intermediates (R^+ and TS_a^+RH, respectively) from reactions which directly create cross-links to those giving cyclic sulphides. Thus, protonation of double bonds vicinal to sulphur attachments by the species R^+ or TS_a^+RH (p. 2878) leads to cyclic sulphide rather than to the cross-linking which directly follows the protonation of other double bonds. In the formation of cyclic sulphide, a carbonium ion is in effect transformed into a persulphenium ion without combination of sulphur. It is this transformation which is held responsible for the lower rate of sulphuration of 1 : 5-dienes compared with comparable mono-olefins,[4] an otherwise peculiar feature of these reactions.

The third point to be made is that the mechanism now proposed for cyclic sulphide formation in a di-isoprene does not readily explain an important feature of the polyisoprene system, *viz.*, the formation of many *isolated* cyclic sulphide structures (*i.e.*, not associated with cross-linking units), as inferred from the low cross-linking efficiency of vulcanisation. Protonation at a double bond vicinal to a polysulphide linkage has been postulated as a prerequisite for formation of a cyclic sulphide. In a polymeric olefin such as natural rubber, random protonation would be expected greatly to outweigh this directed protonation, unless special factors come into play. Two possible factors are: (i) polarisation of specific double bonds, creating an enhanced affinity for protons, by interaction with neighbouring sulphur atoms (*e.g.*, XXXI) (cf. p. 2871); (ii) preferred protonation of the polysulphidic chain, followed by attack of the resultant persulphonium ion (XXXII) at an adjacent double bond (reaction 43) (cf. ref. 27).



(XXXI) (XXXII)

The effect on these reactions of the technologically important "accelerators" and other auxiliary vulcanising agents for rubbers will be discussed elsewhere; a major effect is to increase the importance of persulphenyl anions (TS_b^-) relative to the persulphenium ions in promoting combination of sulphur and in favouring cross-linking.

The work described in this paper and in Parts VIII—X forms part of the programme of research undertaken by the Board of the British Rubber Producers' Research Association.

THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48—56, TEWIN ROAD, WELWYN GARDEN CITY, HERTS. [*Received, December 23rd*, 1957.]

[50] Moore and Ross, unpublished work.
[51] Bloomfield, *J. Soc. Chem. Ind.*, 1949, **68**, 66.

582. *The Reactions of Amines and Sulphur with Olefins. Part IV.*[1] *The Chemical and Thermal Decompositions of* NN′*-Thiobisamines and Their Reactions with Olefins.*

By R. W. Saville.

NN′-Thiobisamines, $(RR'N)_2S_x$ ($x > 1$), undergo N–S bond fission in the presence of hydrogen sulphide, thiols, and other polar reagents. On thermal decomposition at 140° they give the parent amine, hydrogen sulphide, and thioamides, R·NH·CS·R″. *NN*′-Dithiobisdibenzylamine with *cyclo*hexene at 140° gives a complex mixture of mainly saturated sulphides and polymeric sulphides containing benzyl and *cyclo*hexyl groups, together with *N*-benzyl(thiobenzamide) and dibenzylamine. A novel method of olefinic sulphuration with the thiobisamines and hydrogen sulphide is described and the effect of the thiobisamines on interaction of sulphur and olefin is examined. Mechanisms of the thermal decomposition and of the reactions with olefins are discussed.

Parts I—III of this series[1] described the use of combinations of secondary amine and sulphur and of *NN*′-thiobisdiethylamine $Et_2N{\cdot}S{\cdot}NEt_2$ as olefinic sulphurating agents. The introduction[1] of *NN*′-thiobisamines, $(RR'N)_2S_x$, as vulcanising agents for rubber justifies a more detailed study of their properties.

Chemical Decomposition of NN′*-Thiobisamines.*—The reactivity of the N–S bond in sulphenamides, RR′N·SR″, with electrophilic reagents has been studied by several workers,[2] but little attention has been paid to the comparable reactivity of *NN*′-thiobisamines. Blake[3] showed that carbon disulphide and carbon oxysulphide caused N–S bond fission in the thiobisamines and led to thiuram sulphides, $(R_2N{\cdot}CS)_2S_x$, and thiocarbamoyl derivatives, respectively:

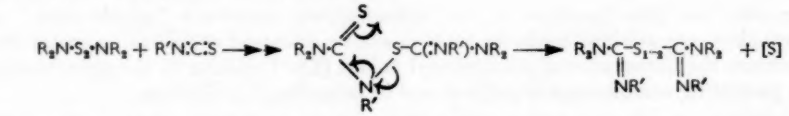
$$R_2N{\cdot}S_x{\cdot}NR_2 + 2CSX \longrightarrow R_2N{\cdot}C(:X){\cdot}S_{x+2}{\cdot}C(:X){\cdot}NR_2$$

In dilute hydrochloric acid the thiobisamines liberate amine, presumably in the manner: $R_2N{\cdot}S_x{\cdot}NR_2 + 2HCl \longrightarrow 2R_2NH + S_xCl_2$, the sulphur halide then yielding sulphur, sulphur dioxide, and hydrogen sulphide.[4] Indicative of preferential N–S, rather than S–S, bond fission in dithiobisamines, $R_2N{\cdot}S_2{\cdot}NR_2$, is Lecher and Weigel's observation,[5] now confirmed, that sulphurous acid affords substances formulated as $[R_2NH^+]_2[S_2O_3H^-]_2$. Treatment in a solvent with hydrogen sulphide rapidly affords sulphur and the parent amine. Similar rapid fission of the N–S bond is observed in the reaction with thiols at room temperature, in the solid state or in ethanol solution, the amine and the tetrasulphide derivative from the thiol being formed in high yield:

$$(C_4H_9ON)_2S_2 + 2C_6H_4Me{\cdot}SH \longrightarrow 2C_4H_9ON + C_6H_4Me{\cdot}S_4{\cdot}C_6H_4Me$$
(C_4H_9ON = morpholine.)

This constitutes a new preparative method for organic tetrasulphides. Thiol-acids with thiobisamines, and thiols with sulphenamides, react similarly, and this is responsible for the catalytic action of thiols on rubber vulcanisation by accelerators containing N–S bonds.

Blake's work[3] has now been extended to *iso*thiocyanates: methyl and benzyl *iso*thiocyanate react readily with dithiobisamines:[6]



[1] Parts I—III, Moore and Saville, *J.*, 1954, 2082, 2089; Glazebrook and Saville, *J.*, 1954, 2094.
[2] *E.g.*, Carr, Smith, and Alliger, *J. Org. Chem.*, 1949, **14**, 921; Chabrier and Renard, *Bull. Soc. chim. France*, 1950, **17**, D13.
[3] Blake, *J. Amer. Chem. Soc.*, 1943, **65**, 1267; U.S.P. 2,368,515/1945.
[4] Cf. Olin, *J. Amer. Chem. Soc.*, 1926, **48**, 167.
[5] Lecher and Weigel, G.P., 520,857/1927.
[6] Cf. Koch, *J.*, 1949, 401.

The effect of Friedel–Crafts catalysts on the N–S bond in thiobisamines has not been examined in detail, but Burg and Woodrow [7] found that boron trifluoride forms stable complexes, presumably by utilisation of the unshared electrons of the nitrogen. The reduction of *NN*-dithiobismorpholine with lithium aluminium hydride gives morpholine, hydrogen sulphide, and sulphur.

Thermal Decomposition of NN′*-Thiobisamines.*—*NN*′-Dithiobisdibenzylamine at 140° *in vacuo* gives dibenzylammonium hydrogen sulphide and *N*-benzyl(thiobenzamide), which are also formed by reaction of dibenzylamine with sulphur at 140° (cf. Moore and Saville [1]):

$$Ph{\cdot}CH_2{\cdot}NH{\cdot}CH_2{\cdot}Ph + 2S \longrightarrow H_2S + Ph{\cdot}CH_2{\cdot}NH{\cdot}CS{\cdot}Ph$$

Hydrogen sulphide and amine are also formed when *NN*′-dithiobis-(2-ethylaminopropionitrile) is heated at 140°, but in this case, and in the reaction of 2-ethylaminopropionitrile with sulphur at 140°, the expected thioamide could not be identified.

Thermal Reaction of NN′*-Thiobisamines with Olefins.*—Negligible reaction occurs between *NN*′-mono- or -di-thiobismorpholine and *cyclo*hexene or 2 : 6-dimethylocta-2 : 6-diene at 140°, in contrast to the extensive reaction [1] of *cyclo*hexene with *NN*′-monothiobisdiethylamine at 140°.

With *cyclo*hexene at 140° *NN*′-dithiobisdibenzylamine yields a complex mixture: (*a*) benzyl *cyclo*hexyl sulphide and mixed sulphides R_2S_x ($R = Ph{\cdot}CH_2$, C_6H_{11}, C_6H_9; $x = 1$—2); (*b*) polymeric sulphides of the type $Ph{\cdot}CH_2{\cdot}S_x{\cdot}C_6H_{10}S_x{\cdot}CH_2{\cdot}Ph$; (*c*) *N*-benzylthiobenzamide; (*d*) dibenzylamine; (*e*) *NN*′-trithiobisdibenzylamine; and (*f*) traces of benzylamine, benzaldehyde, and toluene. Considerable migration of benzyl groups occurs during the above reaction, as in reactions of other benzyl-substituted sulphur compounds, *e.g.*, benzyl alkyl xanthates and benzylsulphonium compounds,[8] and (benzylthio)benzothiazole,[9] and the smooth isomerisation of sulphidimines [8] fails with the dibenzyl compound, $(Ph{\cdot}CH_2)_2S{\cdot}N{\cdot}SO_2{\cdot}Ar$. The monosulphide in fraction (*a*) was identified as its sulphone and by infrared spectroscopy, and the polysulphides in (*b*) by spectroscopy and by reduction with lithium aluminium hydride to toluene-ω-thiol in high yield, together with a polymeric monosulphide analogue and a *cyclo*hexanedithiol, of unknown composition, isolated as its bis-2 : 4-dinitrophenyl sulphide (minor amounts of *cyclo*hexane- and *cyclo*hex-2-ene-thiol were also isolated).

The formation of benzaldehyde, benzylamine, and toluene in the above reactions of *NN*′-dithiobisdibenzylamine is attributed to Willgerodt reactions of the type examined by King and McMillan,[10] and thioamide alkylation: [1]

$$Ph{\cdot}CS{\cdot}NH{\cdot}CH_2{\cdot}Ph + (Ph{\cdot}CH_2)_2NH \longrightarrow Ph{\cdot}CH_2{\cdot}NH_2 + Ph{\cdot}CS{\cdot}N(CH_2{\cdot}Ph)_2$$

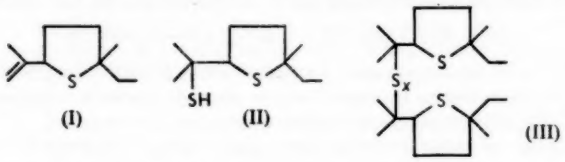
followed by hydrogenolysis of benzyl groups of the amine.[11]

With 1-methyl*cyclo*hexene at 140° *NN*′-dithiobisdibenzylamine gives the thioamide and a high yield of dibenzylamine. The main product had a lower H : C ratio than that of the parent olefin, suggesting the presence of benzyl groups, and its infrared spectrum was consistent with the presence of benzyl 1-methyl*cyclo*hexyl sulphide and di-(1-methyl*cyclo*hexyl) sulphides. Presence of the former was confirmed by oxidation to the sulphone. Hydrogenolysis of the sulphuration product yielded toluene-ω-thiol in large amount, together with a small proportion of 1-methyl*cyclo*hexanethiol and di-(1-methyl*cyclo*hexyl) monosulphide; from the spectral data 2-methyl*cyclo*hexanethiol may also have been present, and the mechanistic significance of this is discussed below.

Olefinic Sulphuration with NN′*-Dithiobisamines and Hydrogen Sulphide.*—The ready interaction of hydrogen sulphide and thiols with *NN*′-dithiobisamines suggests a novel method of olefinic sulphuration. Reaction of 2-methylpent-2-ene with *NN*′-dithiobismorpholine at 20° and 65° was not effected by catalytic amounts of hydrogen sulphide but

[7] Burg and Woodrow, *J. Amer. Chem. Soc.*, 1954, **76**, 219.
[8] Ash, Challenger, and Greenwood, *J.*, 1951, 1877; Ash and Challenger, *J.*, 1952, 2792.
[9] Moore and Waight, *J.*, 1952, 4237.
[10] King and McMillan, *J. Amer. Chem. Soc.*, 1948, **70**, 4145.

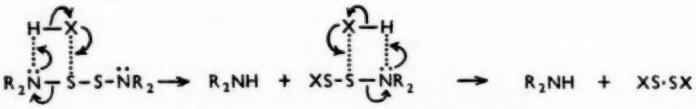
required molar quantities of this agent, and then negligible sulphuration of the olefin occurred. Boiling *cyclo*hexene gave similar results. However, 2 : 6-dimethylocta-2 : 6-diene with *NN'*-dithiobismorpholine and hydrogen sulphide at 140° gave in 1 hour morpholine and a high yield of largely saturated, sulphurated product, in which the ratio of cross-linked polysulphide to cyclic sulphide was considerably greater than was observed for the comparable reaction with sulphur [12] or with sulphur and diethylamine.[1] No detailed analysis of the cyclic sulphide fraction was attempted but the presence of *ca.* 26% of the



(I) (II) (III)

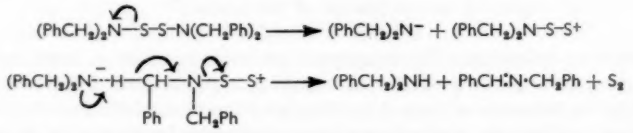
thiophan (I) was indicated by infrared spectroscopy. The polysulphide was mainly saturated, its infrared spectrum being similar to that of compound (II), suggesting that the polysulphide (III) was the major component as similarly obtained from the diene–sulphur–diethylamine reaction.[1] This was confirmed by hydrogenolysis of the polysulphide with lithium aluminium hydride, a thiol similar to (III) being obtained.

Mechanism of the Decomposition of NN'*-Dithiobisamines.*—The formation of amine (R_2NH) by reaction of *NN'*-dithiobisamines, $R_2N{\cdot}S_2{\cdot}NR_2$, with reagents of the type HX (X = Cl, SO_3H, SH, SR') indicates that fission of the N–S bond is an important reaction of this type of compound, *e.g.*:



When HX is a thiol the products are amine and tetrasulphide, but when it is hydrogen sulphide the initially formed H_2S_4 probably forms the salt $R_2NH_2^+HS_4^-$ which decomposes further, particularly in a polar solvent or on treatment with acid, to give sulphur and $R_2NH_2^+HS^-$, as observed experimentally.

The thermal decomposition of *NN'*-dithiobisdibenzylamine to dibenzylamine, hydrogen sulphide, and *N*-benzyl(thiobenzamide) may be explained similarly as involving initial heterolysis of the N–S bond followed by elimination, thus:



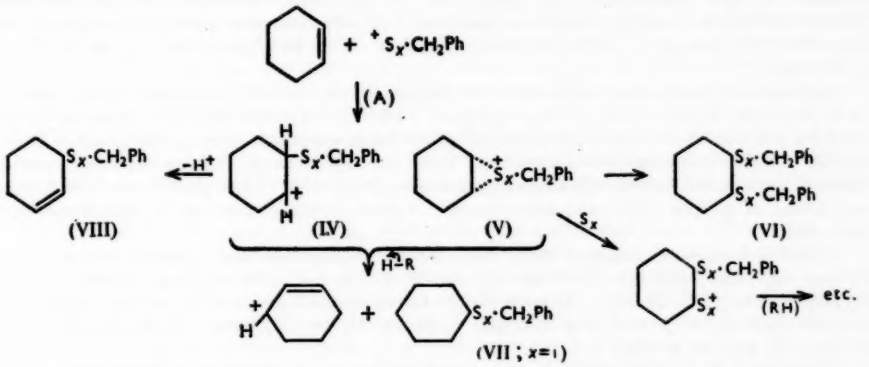
Formation of hydrogen sulphide and *N*-benzylthiobenzamide is then regarded as resulting from (*a*) reaction of the dibenzylamine with sulphur (cf. Moore and Saville [1]), and (*b*) reaction of the benzylidenebenzylamine with sulphur. Although the presence of the Schiff's base in the products could not be proved support for its formation as an intermediate includes (i) the formation of thioamides from Schiff's bases and sulphur,[13] and (ii) the isolation of Schiff's bases in sulphur–amine reaction products.[14]

Isolation of *NN'*-trithiobisdibenzylamine on reaction of the dithiobisamine with *cyclo*hexene at 140° points to disproportionation involving S–S bond fission as an alternative

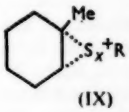
[11] Hartung and Simonoff, "Organic Reactions," Wiley, New York, 1953, Vol. VII, p. 263.
[12] Bateman, Glazebrook, and Moore, *J.*, 1958, 2846.
[13] Kindler, *Annalen*, 1923, **431**, 187; Böttcher and Bauer, *ibid.*, 1950, **568**, 218.
[14] Rosser and Ritter, *J. Amer. Chem. Soc.*, 1937, **59**, 2179.

to some extent to N–S fission. Comparable reactions have been observed with substituted thiuram disulphides, $R_2N{\cdot}CS{\cdot}S{\cdot}S{\cdot}CS{\cdot}NR_2$.

Mechanism of Olefinic Sulphuration with NN'*-Dithiobisdibenzylamine.*—Unlike the reaction of *NN'*-thiobisdiethylamine with *cyclo*hexene [1] that of *NN'*-dithiobisdibenzylamine with olefins yields products which result mainly from the addition of benzylthio-groups to olefinic double bonds, indicating an anomalous course for olefinic sulphuration. The reactions which lead to the formation of the benzylthio-groups remain obscure, but the observed products may result from the electrophilic attack of benzylthio- or benzylpolythio-cations, $Ph{\cdot}CH_2{\cdot}S_x^+$, on the olefin. Thus the major products obtained from *cyclo*hexene, *viz.*, benzyl *cyclo*hexyl sulphide and the polymer $Ph{\cdot}CH_2{\cdot}S_x{\cdot}C_6H_{10}{\cdot}S_x{\cdot}CH_2Ph$ (IV; x = mainly 1), may be formed as shown in the annexed scheme. The intermediate formed from the initial reaction (A) may be assigned either a classical cationic structure (IV) or a π-complex structure (V). Cyclic sulphonium ions of type (V) (cf. Bartlett and Swain [16]) were regarded by Lien, McCaulay, and Proell [17] as chain carriers for the formation



of compounds analogous to the polysulphides (VI) in acid-catalysed reaction of disulphides with olefins, and participation of such intermediates in the present reaction is in conformity with recent mechanistic studies of olefin–sulphur reactions.[18] Formation of the monosulphide (VII) is represented as involving hydride-ion transfer between olefin and (IV—V),[18] which is well known in the analogous Friedel–Crafts reactions.[19] The isolation of a little *cyclo*hex-2-enethiol on hydrogenolysis of the polymeric fraction (*b*) (p. 2881) suggests that a polysulphide (VIII) may be a minor product, formed as shown.



(IX)

The corresponding reaction of the dithiobisamine with 1-methyl*cyclo*hexene (p. 2881) recalls the isolation of 1-methyl*cyclo*hexyl phenyl sulphide on reaction of diphenyl tetrasulphide with 1-methyl*cyclo*hexene.[20] It is believed that these reactions follow the pattern suggested for *cyclo*hexene, proceeding *via* the intermediate sulphonium ion (IX) and leading mainly to tertiary C–S compounds.

Mechanism of Olefinic Sulphuration with Dithiobismorpholine and Hydrogen Sulphide.—Since negligible reaction occurs at 140° between dithiobismorpholine and *cyclo*hexene or 2 : 6-dimethylocta-2 : 6-diene, the ready sulphuration of the diene in the presence of hydrogen sulphide must be due to reaction of the dithiobisamine with hydrogen sulphide.

[15] Craig, Juve, Davidson, Semon, and May, *J. Polymer Sci.*, 1952, **8**, 321.
[16] Bartlett and Swain, *J. Amer. Chem. Soc.*, 1949, **71**, 1406.
[17] Lien, McCaulay, and Proell, Amer. Chem. Soc., General Papers, Pet. Chem. Div., Sept. 1952, No. 28, p. 169.
[18] Bateman, Moore, and Porter, preceding paper.
[19] Baddeley and Pickles, *J.*, 1952, 3726.
[20] Bloomfield, *J.*, 1947, 1547.

XUM

The active sulphurating agent appears to be $C_4H_8ONH_2^+ \cdot HS_4^-$ and the mechanism of sulphuration is probably analogous to that in the amine–sulphur–olefin systems.[1]

The formation of amines by reaction of hydrogen sulphide and thiols with dithiobisamines has been used to confirm the belief [21] that hydrogen sulphide and thiols are not intermediates in sulphur–olefin reactions. It was found that *cyclo*hexene and sulphur at 140° in the presence of dithiobismorpholine yield the normal olefinic polysulphide obtained also in the absence of the dithiobisamine and that morpholine formation is negligible.

Experimental

Preparation of NN′-*Dithiobisamines.*—NN′-*Dithiobisdibenzylamine*, obtained (92%) from dibenzylamine and sulphur monochloride by Throdahl and Harman's method,[22] crystallised from alcohol–light petroleum in pale yellow needles, m. p. 79—80° (Found: C, 73·5; H, 6·1; N, 6·05. $C_{28}H_{28}N_2S_2$ requires C, 73·7; H, 6·1; N, 6·1%). *NN′*-Dithiobismorpholine was obtained similarly (82%) as colourless needles [from ethanol–ethyl acetate (10 : 1)], m. p. 125° (Found: S, 27·0. Calc. for $C_8H_{16}O_2N_2S_2$: S, 27·1%). *NN′*-Dithiobis-(β-ethylaminopropionitrile) was obtained (66%) by Harman's method [23] as colourless prisms (from ethanol–acetone), m. p. 77—79° (Found: C, 46·8; H, 6·85; N, 21·2. Calc. for $C_{10}H_{18}N_4S_2$: C, 46·5; H, 7·0; N, 21·7%).

Preparation of Reference Compounds.—*N*-Benzyl(thiobenzamide), m. p. 84—85° (Found: C, 73·8; H, 5·75; N, 6·2. Calc. for $C_{14}H_{13}NS$: C, 74·0; H, 5·7; N, 6·2%), was prepared in 52% yield by reaction of *N*-benzylbenzamide (10 g.) with phosphorus pentasulphide (5 g.) in boiling xylene. It was recovered unchanged after 10 hr. at 140° *in vacuo*; it was not hydrolysed by dilute mineral acids, but in refluxing sulphuric acid (70% w/w) (1 hr.) gave benzoic acid, m. p. and mixed m. p. 120—121°, and benzylamine, isolated as the picrate, m. p. and mixed m. p. 193—194°.

cyclo*Hex*-2-*enethiol*, obtained (69%) from 3-bromo*cyclo*hexene and thiourea, had b. p. 44°/11 mm., n_D^{20} 1·5230 (Found: C, 63·65; H, 8·8; S, 27·35; SH, 28·4. $C_6H_{10}S$ requires C, 63·2; H, 8·8; S, 28·0; SH, 29·0%). It gave the 2 : 4-*dinitrophenyl derivative* as yellow prisms (from ethanol–acetone), m. p. 114—115° (Found: C, 51·55; H, 4·6; N, 10·05. $C_{12}H_{12}O_4N_2S$ requires C, 51·4; H, 4·3; N, 10·0%).

Thiophenol (11 g., 0·1 mole) was added with stirring to a solution of sodium (2·3 g., 0·1 g.-atom) in ethanol (40 ml.) under nitrogen, followed by 3-bromo*cyclo*hexene (16·1 g., 0·1 mole) in ethanol (15 ml.). After being warmed for 30 min. the mixture was poured into water, and extracted with ether, and the extract was washed with water, dried (K_2CO_3), and fractionated, to give *cyclo*hex-2-enyl phenyl sulphide, b. p. 89—90°/0·01 mm., n_D^{20} 1·5920 (79%) (Found: C, 75·35; H, 7·3; S, 16·65. Calc. for $C_{12}H_{14}S$: C, 75·8; H, 7·4; S, 16·8%).

Phenyl*cyclo*hexyl sulphide, b. p. 111°/0·1 mm., n_D^{20} 1·5680, was prepared by Cunneen's method.[24] The corresponding sulphone had m. p. 73—74°.

*cyclo*Hexene (15 g.), toluene-ω-thiol (30 g.), and ascaridole (0·1 g.) were refluxed on the steam-bath for 7 hr. and the product was fractionated, to give benzyl *cyclo*hexyl sulphide, b. p. 88—89°/0·01 mm., n_D^{22} 1·5556 (45%) (Found: C, 75·4; H, 8·7; S, 15·4. Calc. for $C_{13}H_{18}S$: C, 75·7; H, 8·7; S, 15·6%), which with peracetic acid gave the sulphone, colourless flakes from (ethanol–light petroleum), m. p. 100—101° (Found: C, 65·4; H, 7·55; S, 13·25. Calc. for $C_{13}H_{18}O_2S$: C, 65·5; H, 7·5; S, 13·4%).

Attempts to prepare 1 : 2-epithio*cyclo*hexane from 1-chloro-2-thiocyanato*cyclo*hexane and sodium sulphide [25] gave mainly a polymer, as expected for the alkaline conditions used,[26] and a thiol. Reduction of the polymer with lithium aluminium hydride gave the same thiol, b. p. 48—50°/0·1 mm., n_D^{20} 1·5410 (Found: C, 51·1; H, 8·25; S, 37·1. Calc. for $C_6H_{12}S_2$: C, 48·6; H, 8·1; S, 43·2%), which contained *cyclo*hexane-1 : 2-dithiol since on reaction with benzaldehyde and hydrogen chloride it gave the dithiolan,[27] m. p. 115°, and with potassium methyl

[21] Ross, *J.*, 1958, 2856.
[22] Throdahl and Harman, *Ind. Eng. Chem.*, 1951, **43**, 421.
[23] Harman, U.S.P. 2,649,470; B.P. 708,627; B.P. 711,236.
[24] Cunneen, *J.*, 1947, 36.
[25] Farmer and Shipley, *J.*, 1947, 1519.
[26] Culvenor, Davies, and Heath, *J.*, 1949, 282.
[27] Cf. Culvenor and Davies, *Austral. J. Sci. Res.*, 1948, **1**, *A*, 236.

xanthate gave the *cyclo*hexyl trithiocarbonate,[28] m. p. 169°. Attempts to prepare a solid 2 : 4-dinitrophenyl sulphide derivative of the dithiol were unsuccessful.

Benzyl 1-methyl*cyclo*hexyl sulphide was prepared by Moore and Saville's method.[1] On oxidation with peracetic acid it gave the *sulphone* as flakes [from light petroleum–ethanol (10 : 1)], m. p. 100° (Found: C, 67·1; H, 8·0; S, 12·6. $C_{14}H_{20}O_2S$ requires C, 66·7; H, 7·9; S, 12·7%).

Chemical Decompositions of NN′*-Dithiobisamines.*—*NN′*-Dithiobisdibenzylamine (2·0 g.) was shaken vigorously with 15% sulphurous acid (50 ml.) and then cooled to 0° for 2 days. The S_4*-compound* separated (2·7 g.) and formed colourless prisms, m. p. 143—144°, from ethanol (Found: C, 53·55; H, 5·0; N, 4·25; S, 20·45. $C_{28}H_{32}N_2O_6S_4$ requires C, 54·2; H, 5·15; N, 4·5; S, 20·7%).

The same *NN′*-dithiobisamine was decomposed by warm dilute mineral acids to sulphur, hydrogen sulphide, sulphur dioxide, and the parent amine, identified as picrate.

A benzene solution of the *NN′*-dithiobisamine with hydrogen sulphide gave a red insoluble oil and sulphur; the decomposition was favoured by the presence of polar solvents.

NN′-Dithiobismorpholine (11·8 g., 0·05 mole) and toluene-*p*-thiol (12·4 g., 0·1 mole) were mixed as fine powders at room temperature: a rapid reaction ensued, the mixture becoming yellow, liquid, and finally deep red, with the evolution of a small amount of hydrogen sulphide. After 3 hr. the product was fractionated to give morpholine (5·8 g.), b. p. 25—30°/10 mm., n_D^{20} 1·4560 (identified as picrate, m. p. 146—147°), and a residual yellow oil (14·9 g.), undistillable at 140°/0·01 mm., which was devoid of thiol and appeared to be principally di-*p*-tolyl tetrasulphide (13·2 g.) (Found: C, 53·05; H, 4·7; S, 40·65. Calc. for $C_{14}H_{14}S_4$: C, 54·2; H, 4·5; S, 41·3%). Use of a solvent (*e.g.*, ethanol) gave a more controllable reaction and minimised side reactions leading to hydrogen sulphide. Other thiols reacted similarly. Comparable reactions between sulphenamides and thiols were less vigorous owing to the intermediate formation of the solid amine–thiol salt.

NN′-Dithiobisdibenzylamine (9·1 g., 0·02 mole) was unchanged when refluxed for 2 hr. with lithium aluminium hydride (1·9 g., 0·05 mole) in ether (200 ml.). The *NN′*-dithiobisamine (9·1 g.) in tetrahydrofuran (20 ml.) was then refluxed for 4 hr. with the reagent (3·0 g.) in tetrahydrofuran (50 ml.). Decomposition with ice and 2N-sulphuric acid gave hydrogen sulphide and a white solid (apparently dibenzylammonium sulphate) which was treated with alkali to yield dibenzylamine, isolated as its hydrochloride (4·5 g. equiv. to 3·8 g. of amine). The original ether extract gave only impure sulphur (>0·8 g.). The starting material was stable to cold 2N-sulphuric acid.

[With Dr. G. H. Thomas].—(i) A mixture of *NN′*-dithiobismorpholine (3·0 g.) and methyl *iso*thiocyanate (2·5 g.) in benzene (20 ml.) was heated *in vacuo* for 8 hr. at 140°, giving sulphur and *di-(α-methylimino-α-morpholinomethyl) sulphide*, prisms (from ethanol), m. p. 150—151° Found: C, 50·45; H, 7·9; N, 20·0; S, 11·55. $C_{12}H_{22}O_2N_4S$ requires C, 50·3; H, 7·7; N, 19·6; S, 11·2%). (ii) A comparable reaction to (*i*), with benzyl *iso*thiocyanate, gave *di-(α-benzylimino-α-morpholinomethyl) disulphide*, plates (from benzene), m. p. 98° (Found: C, 61·1; H, 6·8; N, 11·95; S, 13·35. $C_{24}H_{30}O_2N_4S_2$ requires C, 61·3; H, 6·4; N, 11·9; S, 13·6%).

Thermal Decomposition of NN′*-Dithiobisdibenzylamine.*—(i) When this compound, m. p. 80°, was heated under nitrogen for 5 hr. at 140° no hydrogen sulphide was evolved and the product (Found: C, 73·55; H, 6·15%) had m. p. and mixed m. p. with the original compound, 70—71°, indicating possible disproportionation. (ii) The dithiobisamine (5·0 g.) was heated *in vacuo* for 20 hr. at 140° ± 1°: hydrogen sulphide was formed, together with *N*-benzyl(thiobenzamide) (2·1 g.), m. p. 83—84° (Found: C, 74·2; H, 6·1; N, 6·2. Calc. for $C_{14}H_{13}NS$: C, 74·0; H, 5·7; N, 6·2%). (iii) The dithiobisamine (9·1 g.) was heated in nitrogen for 24 hr. at 140° ± 1°, then treated in ether with hydrogen chloride, to give dibenzylammonium hydrochloride. Evaporation of the solution gave *N*-benzyl(thiobenzamide) (6·1 g.), m. p. 81—83° (Found: C, 74·1; H, 5·7; N, 6·2%).

Reaction of Dibenzylamine with Sulphur.—The amine (10·3 g.) and sulphur (2·0 g.) were heated *in vacuo* for 24 hr. at 140° ± 1° with shaking, then cooled to −10° for 2 days. *N*-Benzylthiobenzamide (4·2 g.), m. p. and mixed m. p. 84—85° (Found: C, 73·7; H, 5·9; N, 6·4%), separated. Evaporation of the filtrate gave dibenzylammonium hydrogen sulphide, m. p. (sealed tube) 32—34° (cf. Achterhof [29]).

[28] Culvenor, Davies, and Pausacker, *J.*, 1946, 1050.
[29] Achterhof, *J. Amer. Chem. Soc.*, 1931, **53**, 2687.

XUM

Thermal Decomposition of NN'-*Dithiobis*-(*α-ethylaminopropionitrile*).—Heating the compound *in vacuo* for 10 hr. at 140° ± 1° gave traces of the hydrogen sulphide of β-ethylaminopropionitrile and a tar.

Reaction of α-Ethylaminopropionitrile with Sulphur.—Heating the amine (9·8 g.) with sulphur (3·2 g.) *in vacuo* for 10 hr. at 140° ± 1° gave the amine hydrogen sulphide and tar.

Reaction of NN'-*Dithiobisdibenzylamine with* cyclo*Hexene.*—(1) The dithiobisamine (34·2 g., 0·075 mole) and the olefin (61·5 g., 0·75 mole) were heated *in vacuo* for 24 hr. at 140° ± 1°. The red-brown liquid yielded no crystals at −10° (1 week). Unchanged olefin (36 g.) was removed and to the residue was added light petroleum (250 ml.). A dark oil (~5 g.) separated, which crystallised at low temperature, the solid product being *N*-benzyl(thiobenzamide), obtained as light yellow needles on repeated crystallisation (charcoal) from aqueous ethanol (m. p. and mixed m. p. 82—83·5°) (Found: C, 73·5; H, 5·75; N, 6·1%). Treatment of the petroleum solution with 2N-hydrochloric acid (150 ml.) gave dibenzylammonium hydrochloride (12·0 g.). This was removed, and the filtrate re-extracted with acid, washed with water, dried ($CaCl_2$), and evaporated, to give the olefinic sulphuration product (i) (33 g.) (Found: C, 72·65; H, 7·55; N, 1·3%; C : H, 6 : 7·5). Fractional distillation of this gave (ii) 2 : 4-dinitrotoluene, m. p. 70° (*ca.* 1 g.), (iii) a liquid, b. p. 88°/0·001 mm., n_D^{20} 1·5500 (5·7 g.) (Found: C, 73·7; H, 9·0; N, 0·07; S, 17·15%), and (iv) a deep red oil (15·3 g.), undistillable at 140°/0·001 mm. (Found: C, 71·0; H, 6·85; N, 1·89%) which at 0° slowly deposited a trace of *N*-benzyl(thiobenzamide).

Infrared spectroscopic analysis of fraction (iii) showed that the principal constituent (70%) was benzyl *cyclo*hexyl sulphide, by comparison with a synthetic sample. Refractionation gave (iii*a*) b. p. 78—80°/0·01 mm., n_D^{20} 1·5470 (4·0 g.) (Found: C, 74·0; H, 9·25; S, 16·2%; C : H, 6 : 9), and (iii*b*) b. p. 82—86°/0·01 mm., n_D^{20} 1·5665 (0·8 g.) (Found: C, 71·35; H, 8·65; S, 19·6%; C : H, 6 : 8·7). Infrared analysis of fractions (iii*a* and *b*) revealed benzyl *cyclo*hexyl sulphide as the main component, only small amounts of di*cyclo*hexyl and di*cyclo*hex-2-enyl sulphide being present. The presence of benzaldehyde in fractions (iii) and (iii*a* and *b*) was established by a band at 1710 $cm.^{-1}$ due to C=O in their infrared spectra, and by formation of benzaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 234—235°. Oxidation of fraction (iii) with peracetic acid gave benzyl *cyclo*hexyl sulphone, m. p. and mixed m. p. 100—101° (Found: C, 65·3; H, 7·55; S, 13·6. Calc. for $C_{13}H_{18}O_2S$: C, 65·5; H, 7·5; S, 13·4%). No other crystalline sulphone could be identified.

Extraction of a benzene solution of fraction (iv) with 10% sulphurous acid failed to give any S_4-derivative, indicating the absence of the dithiobisamine. [In an independent experiment, treatment of a benzene solution of the dithiobisamine with 10% sulphurous acid gave the S_4-compound (93%).] The benzene solution of fraction (iv) was washed with aqueous sodium hydrogen carbonate, then with water, dried, and eluted through alumina, to give fraction (v) (Found: C, 66·9; H, 6·15; N, 1·8; S, 25·2%; C : H, 6 : 6·6). A solution of this fraction (14·0 g.) was refluxed with stirring with lithium aluminium hydride (5·0 g.) in ether (250 ml.) for 2 hr., then decomposed with ice and 2N-sulphuric acid. Removal of the solvent and fractionation gave: (v*a*) impure *cyclo*hex-2-enethiol, b. p. 40°/10 mm., n_D^{25} 1·5070 (0·5 g.) (Found: C, 62·75; H, 9·2; S, 26·6; SH, 28·8%; C : H, 6 : 10·5. Calc. for $C_6H_{10}S$: C, 63·2; H, 8·8; S, 28·0; SH, 29·0%) (its infrared spectrum indicated >40% of the thiol; it gave 2 : 4-dinitrophenyl *cyclo*hex-2-enyl sulphide (m. p. 115°, mixed m. p. 114—115°); (v*b*) b. p. 60—80°/10 mm., n_D^{25} 1·5460 (2·1 g.) (Found: C, 65·8; H, 7·6; S, 25·35%; C : H, 6 : 8·4) [shown by infrared analysis to contain toluene-ω-thiol (70%) identified as its 2 : 4-dinitrophenyl derivative, m. p. and mixed m. p. 128—129° (Found: C, 53·4; H, 3·45; N, 9·4. Calc. for $C_{13}H_{10}O_4N_2S$: C, 53·8; H, 3·45; N, 9·7%); the presence of *cyclo*hexanethiol was demonstrated by the formation of 2 : 4-dinitrophenyl *cyclo*hexyl sulphide, m. p. and mixed m. p. 145·5—147°]; (v*c*) b. p. 35°/0·01 mm., n_D^{25} 1·5645 (1·1 g.) (Found: C, 59·65; H, 7·4; S, 32·25%; C : H, 6 : 8·9) [shown by infrared analysis to consist mainly of benzyl *cyclo*hexyl sulphide (or material of the type $Ph{\cdot}CH_2{\cdot}S{\cdot}C_6H_{10}{\cdot}S{\cdot}CH_2Ph$) together with toluene-ω-thiol, identified as the 2 : 4-dinitrophenyl derivative, m. p. and mixed m. p. 125—127° (Found: C, 53·45; H, 3·5; N, 9·8%), and a *cyclo*hexanedithiol of unknown composition characterised as its bis-2 : 4-dinitrophenyl derivative, m. p. 193—194·5° (Found: C, 45·5; H, 3·45; N, 11·35. Calc. for $C_{18}H_{14}O_8N_4S_2$: C, 45·1; H, 3·34; N, 11·7%)]; (v*d*), b. p. 84—88°/0·01 mm., n_D^{25} 1·5590 (0·65 g.) (Found: C, 69·1; H, 8·4; S, 21·8%; C : H, 6 : 8·7) [shown by infrared analysis to be mainly benzyl *cyclo*hexyl sulphide and $Ph{\cdot}CH_2{\cdot}S{\cdot}C_6H_{10}{\cdot}S{\cdot}CH_2Ph$, but containing also a *cyclo*hexanedithiol characterised

as its bis-2 : 4-dinitrophenyl derivative, m. p. 195—196°]; and (*ve*) a residue (7·8 g.) undistillable at 140°/0·001 mm. Chromatography of (*ve*) (7·0 g.) in light petroleum gave (*vf*) a light yellow oil (1·8 g.) [Found: C, 74·1; H, 7·65; N, 1·35%; C : H, 6 : 7·4; *M* (ebullioscopic in C_6H_6), 294, 303)], and further elution with light petroleum–ethanol (19 : 1) gave (*vg*) a yellow oil (4·0 g.) [Found: C, 78·75; H, 7·35; N, 3·0%; C : H, 6 : 7; *M* (as above), 362, 372]. Infrared examination of fractions (*vf* and *g*) indicated the presence of benzyl and *cyclo*hexyl groups suggestive of the presence of $Ph{\cdot}CH_2{\cdot}S{\cdot}C_6H_{10}{\cdot}S{\cdot}CH_2Ph$ and apparently traces of *N*-benzyl(thiobenzamide), but definitely precluded the presence of tetrabenzylhydrazine.

(2) Reaction of *NN'*-dithiobisdibenzylamine (22·8 g.) with *cyclo*hexene as above gave a fraction (0·65 g.) which was almost pure benzylamine, b. p. 35°/0·2 mm., n_D^{20} 1·5425 (Found: C, 78·15; H, 8·4; N, 12·5; S, 1·0. Calc. for C_7H_9N: C, 78·5; H, 8·4; N, 13·0%), identified as its picrate, m. p. 198—199° (Found: C, 46·25; H, 3·5; N, 16·9. Calc. for $C_{13}H_{12}O_7N_4$: C, 46·4; H, 3·6; N, 16·7%).

(3) The dithiobisamine (17·1 g.) and olefin (36·9 g.) were heated *in vacuo* for 10 hr. at 140° ± 1°. The product, which contained no tar, was freed from volatile material, and the residue (20·7 g.) cooled to 0°: it partially crystallised. Filtration gave a solid (10·1 g.) which crystallised from light petroleum (charcoal) in prisms, m. p. 72—73° (Found: C, 71·05; H, 5·8; N, 5·65%). Fractionation from light petroleum then gave NN'-*trithiobisdibenzylamine* as prisms (from light petroleum or ethanol–ethyl acetate), m. p. 109—111° (Found: C, 68·85; H, 5·7; N, 5·37; S, 19·5. $C_{28}H_{28}N_2S_3$ requires C, 68·8; H, 5·7; N, 5·7; S, 19·7%). Examination of the more soluble fractions failed to yield any *NN'*-monothiobisdibenzylamine.

Reaction of NN'-*Dithiobisdibenzylamine with* 1-*Methyl*cyclo*hexene.*—A similar procedure to that followed in the *cyclo*hexene reaction was used. The main experimental findings are summarised on p. 2881.

Formation of Morpholine from 2-*Methylpent*-2-*ene,* NN'-*Dithiobismorpholine, and Hydrogen Sulphide.—General Procedure.* The *NN'*-dithiobisamine (5·9 g., 0·025 mole) and the olefin (0·25 mole) were stirred rapidly at 20° or 65° for 1 hr. while either a trace or a steady stream of hydrogen sulphide was introduced. After removal of solid *NN'*-dithiobisamine and/or sulphur, the solution was freed from olefin and the residue fractionated or titrated directly in aqueous ethanol against standard hydrochloric acid to determine the yield of morpholine (identified as its picrate) (see Table). In two control experiments the olefin was replaced by ethanol and by light petroleum.

Expt. no.	1	2	3	4	5	6	7
Olefin	†	†	†	0	0	†	†
H_2S	0	Tr	†	†	†	Tr	†
Temp.	65°	65°	65°	65°	65°	20°	20°
Other solvent	—	—	—	Pet	EtOH	—	—
Yield (g.) of morpholine	0·0	0·1	2·8	0·67	1·3	0·4	0·4
NN'-Dithiobisamine recovered (g.)	5·6	5·45	—	—	—	—	—

† = Excess. Tr = trace. Pet = light petroleum.

Reaction of 2 : 6-*Dimethylocta*-2 : 6-*diene with* NN'-*Dithiobismorpholine in Absence and in Presence of Hydrogen Sulphide.*—(1) The olefin (25·0 g.) and the dithiobisamine (12·6 g.), refluxed under nitrogen for 1 hr. at 140°, gave a reddish-brown product, with no indications of amine hydrogen sulphide or of hydrogen sulphide formation. On cooling, unchanged dithiobisamine (8·8 g.) separated. Filtration and washing the filtrate with ice-cold light petroleum gave further dithiobisamine (1·8 g., total 85%).

(2) A stirred mixture of the olefin (25·0 g.) and the dithiobisamine (12·6 g.) was refluxed under nitrogen at 140° and hydrogen sulphide introduced during 1 hr. Morpholine hydrogen sulphide separated. The reddish-brown product was decanted from tar (2 g.) and fractionated to give fractions: (i) b. p. 36—50°/10 mm., n_D^{20} 1·4525 (6·5 g.) (Found: C, 54·9; H, 10·9; N, 11·43%), containing morpholine (picrate, m. p. 146—147°); (ii) b. p. 60—80°/10 mm., n_D^{20} 1·4535 (16·8 g.) (Found: C, 86·75; H, 10·85; N, 1·35%; C : H, 10 : 18), unchanged olefin containing a little morpholine (picrate, m. p. 146—147°); (iii) unchanged olefin plus cyclic sulphide, b. p. 89—92°/10 mm., n_D^{20} 1·4870 (0·9 g.) (Found: C, 77·0; H, 11·5; N, 0·07%; C : H, 10 : 18); (iv) evaporative distillate (1·7 g.) (Found: C, 56·1; H, 8·4; N, 0%; C : H, 10 : 18); (v) residue (5·0 g.) which on elution in benzene through alumina and removal of solvent gave a polysulphide (Found: C, 49·4; H, 7·45; N, 0·01%; C : H, 10 : 18). Infrared analysis confirmed the presence of morpholine and unchanged olefin in fractions (i) and (ii) and revealed the

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presence of ~26% of $CH_2{:}CRR'$ in (iii) indicative of the cyclic sulphide; fraction (iv) contained $R{\cdot}CH{:}CRR'$ groups (band at 830 $cm.^{-1}$) but the major polysulphide fraction (v) was saturated (compound III). Fraction (v) showed no absorption maximum near 4000 Å, the absorption being consistent with that of a saturated polysulphide. A portion (4·0 g.) of fraction (v) in ether was reduced with lithium aluminium hydride (1·5 g.) in the usual manner and the product fractionated to give materials: (v*a*) b. p. 60°/0·1 mm., n_D^{20} 1·5110 (0·7 g.) (Found: C, 61·8; H, 10·1; S, 27·5; SH, 20·3%; C : H, 10 : 19·6); (v*b*) b. p. 78—80°/0·1 mm., n_D^{20} 1·5275 (0·9 g.) (Found: C, 56·85; H, 9·45; S, 28·9; H, 25·2%; C : H, 10 : 20); and (v*c*), a residue, which on elution in light petroleum (b. p. 40—60°) through alumina gave a polysulphide as an orange-red oil (Found: C, 58·05; H, 9·6; S, 28·8; C : H, 10 : 19·8. Calc. for $C_{20}H_{40}S_4$: C, 58·8; H, 9·8; S, 31·4%). The infrared spectra of (v*a* and *b*) showed strong resemblances to that of the thiol-cyclic sulphide (II), (v*a*) containing also traces of unsaturated material; the infrared spectrum of (v*c*) was similar to those of (v*a* and *b*).

Influence of NN'-*Dithiobismorpholine on the Sulphur–*cyclo*Hexene Reaction.—cyclo*Hexene (41 g., 0·5 mole), sulphur (4·8 g., 0·15 g.-atom), and the dithiobisamine (11·8 g., 0·05 mole) were heated *in vacuo* for 5 hr. at 140° ± 1°. The deep red liquid product was decanted from tar (1 g.) and fractionated to give: (i) impure morpholine, b. p. 40°/10 mm., n_D^{20} 1·4600 (0·6 g.) (Found: C, 56·3; H, 10·6; N, 14·4. Calc. for C_4H_9ON: C, 55·2; H, 10·35; N, 16·1%; (ii) dithiobisamine, b. p. 60°/0·001 mm. (1·2 g.); and (iii) a residue (16 g.) which was extracted from benzene, with 0·1N-hydrochloric acid, washed with water, extracted with sulphurous acid, washed, dried, eluted through alumina, and fractionated to give a polysulphide (10·5 g.) containing a trace of the dithiobisamine (Found: C, 53·45; H, 7·0; N, 0·5%; C : H, 6 : 9·4).

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NOTES.

583. *Catalytic Hydrogenation of Unsaturated Sulphides and Sulphones.*

By L. Bateman and F. W. Shipley.

High-pressure hydrogenation of organic sulphides over heavy-metal oxides or sulphides has the disadvantage that extensive hydrogenolysis usually occurs at the high temperatures required. Although there are exceptions to this, *e.g.*, thiophen and allyl phenyl sulphide have been reduced without appreciable C–S bond fission at 150—250°/2000 lb. per sq. in. in the presence of rhenium heptasulphide,[1] the hydrogenolysis and the inability to measure hydrogen absorption quantitatively with small samples make it desirable to develop less vigorous and more precise low-pressure methods.

By means of palladium on charcoal or barium sulphate, thiophen and certain of its derivatives have been reduced [2] at room temperature at 20—25 lb. per sq. in. and the same catalyst (on charcoal) has been used for the reduction of 1-methylallyl phenyl sulphide [3] and allyl and phenyl propenyl sulphide [4] at room temperature and pressure. For a range of sulphides and some sulphones we find the following generalizations: (i) Simple acyclic allylic or vinylic sulphides absorb hydrogen less readily than related olefins, but do so

[1] Broadbent, Slaugh, and Jarvis, *J. Amer. Chem. Soc.*, 1954, **76**, 1519.
[2] Mozingo, Harris, Wolf, Hoffhine, Easton, and Folkers, *ibid.*, 1945, **67**, 2092.
[3] Cope, Morrison, and Field, *ibid.*, 1950, **72**, 66.
[4] Tarbell and McCall, *ibid.*, 1952, **74**, 48.

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completely in about one hour. (ii) Substitution in the allyl unit greatly reduces the initial rate and also the extent of reaction. (iii) Heterocyclic unsaturated sulphides react more readily than their acyclic analogues, but the effect of substitution noted in (ii) also operates, markedly so for the tetra-substituted double bond in 2 : 3-dimethylthia*cyclo*hex-2-ene. (iv) Unsaturated sulphones react much more readily than the corresponding sulphides,[3,5] but increased alkyl-substitution at the double bond or adjacent to the

Hydrogenation on palladium–charcoal.

Compound	Remarks
Olefins.	
*cyclo*Hexene	Rapid; complete in 5—10 min.
1-Methyl-2-1′-methyl*cyclo*hexyl*cyclo*hexene	Complete in 15 hr.
Acyclic allyl and vinyl sulphides.	
CH_2:CH·CH_2·SBu^n	Complete in 1 hr.
CH_2:CH·CH_2·SPh	Somewhat variable; complete in 1—3 hr.
$(CH_2$:CH·$CH_2)_2$S	50% in 18 hr.; some hydrogenolysis to thiol
Me·$[CH_2]_5$·CH:CH·SMe	Complete in 2—3 hr.
Me·$[CH_2]_5$·CH:CH·SEt	Complete in 4 hr.
Acyclic monosubstituted allyl sulphides.	
CH_2:CH·CHMe·SBu^n	94% in 23 hr.
CHMe:CH·CH_2·SBu^n	Complete in 35—45 hr.
CHMe:CH·CH_2·SPh	75% in 2 days, 100% in 5 days (trace of thiol formed)
CHPh:CH·CH_2·SPh	Very slow; 35% in 4 days (thiol formed)
Disubstituted allyl sulphides.	
CHMe:CH·CHMe·SBu^n	33% in 48 hr. (thiol formed)
CHMe:CH·CHMe·SMe	30% in 18 hr. (thiol formed)
CHMe:CH·CHMe·SPh	25% in 20 hr. (thiol formed)
3-Methylthio*cyclo*hexene	40% in 24 hr.
3-*iso*Propylthio*cyclo*hexene	20% in 17 hr.
Heterocyclic sulphides.	
2 : 5-Dihydrothiophen	100% in 12 min.
Thia*cyclo*hex-2-ene	100% in 15 min.
Thia*cyclo*hex-3-ene	90% in 18 hr.
2 : 3-Dihydro-5-methyl-2-*iso*propylthiophen	100% in 35 min.
2 : 3-Dihydrothia*cyclo*hex-2-ene	Very slow; 98% in 10 days
Sulphones.	
$(CH_2$:CH·$CH_2)_2SO_2$	All rapid; 100% in 8—15 min.
CHPh:CH·CH_2·SO_2·Ph	
*cyclo*Hex-2-enyl methyl sulphone	
2 : 5-Dihydrothiophen 1 : 1-dioxide	
2 : 3-Dihydro-5-methyl-2-*iso*propylthiophen 1 : 1-dioxide	
CHMe:CH·CHMe·SO_2·Ph	90% in 15 min., 100% in 1 hr.
2 : 3-Dimethylthia*cyclo*hex-2-ene 1 : 1-dioxide	Much slower; 100% in 2—3 hr. (no thiol detected)
tert.-Butyl *cyclo*hex-2-enyl sulphone	Very slow; 100% in 9 days (thiol formed)
CHMe:CH·CHMe·SO_2·Bu^n	Very slow; 26% in 5 days (thiol formed)
Miscellaneous	
CH_2:CH·CH_2·SO·Ph	Very slow (PhSH formed)
Me·CH(SMe)·CH:CH·SMe	Very slow; complete in 10 days
N-(2-Methylthia*cyclo*hex-2-en-1-yl)toluene-*p*-sulphonylimide	2 mol. H_2 (*i.e.*, hydrogenolysis + hydrogenation) in 1 hr.

sulphone group is again deactivating, in some cases severely. (v) Concomitant hydrogenolysis with liberation of thiol inhibits hydrogenation; this " poisoning effect " can be partly offset by the addition of strong bases, but these also reduce the activity of the catalyst.

Since unsaturated and the corresponding saturated sulphides can generally be separated chromatographically, even partial reduction with the minimum of side reactions provides a useful procedure for analysis and identification.[6]

[5] Backer and Strating, *Rec. Trav. chim.*, 1937, **56**, 1069.
[6] Bateman, Glazebrook, and Moore, *J.*, 1958, 2846.

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Experimental.—The palladium chloride–Norite catalyst was prepared by a standard method.[7] For each run, 3·0 g. of catalyst, containing 1·4 millimoles of palladium chloride, was hydrogenated in absolute ethanol (15 ml.), and the resulting palladium–charcoal was washed free from hydrochloric acid on a filter funnel, and again shaken with hydrogen in the hydrogenation vessel until no further absorption occurred. The unsaturated compound (*ca.* 10 millimoles) in absolute ethanol (5—10 ml.) was then added, and hydrogenation carried out at room temperature and atmospheric pressure under vigorous agitation. Results are tabulated.

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[7] *Org. Synth.*, **26**, 78 (Catalyst C).

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584. *An Exchange Reaction of Arenesulphenyl Chlorides with Organic Disulphides.*

By C. G. Moore and M. Porter.

Arenesulphenyl chlorides (I) have been shown to undergo an exchange reaction with disulphides (II) (R = aryl, aralkyl, alkyl) to give unsymmetrical disulphides (III) (reaction 1*a*):

$$\underset{(I)}{ArSCl} + \underset{(II)}{RS{\cdot}SR} \underset{b}{\overset{a}{\rightleftharpoons}} \underset{(III)}{ArS{\cdot}SR} + \underset{(IV)}{RSCl} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Reaction occurs readily at room temperature in acetic acid solution, the product (III) often crystallising after a few days (see Table), but is slower in less polar solvents (ether, carbon tetrachloride, xylene). Experiments were confined to chlorides (I) in which Ar = 2 : 4-dinitrophenyl or 4-carboxy-2-nitrophenyl, but the reaction is likely to be general. An equilibrium (1*a* $\rightleftharpoons$ 1*b*) probably exists in a homogeneous system and this is supported by the facts that: (i) under anhydrous conditions, where competitive hydrolysis of the sulphenyl halides (I) and (IV) is absent, the reactants (I) and (II) were still present after long reaction periods; and (ii) quantitative yields of the product (III) [the stoicheiometric completion of (1*a*) being assumed] were not obtained. While the chloride (IV) was not identified it was shown that negligible loss of the sulphenyl halide group occurred under anhydrous conditions.

Reactions (2) and (3) should, in principle, compete with (1*a*, *b*), (2) giving the symmetrical diaryl disulphide (V). No evidence was obtained for reaction (2) when the chloride (I; Ar = 2 : 4-dinitrophenyl) was used in 100% excess over the disulphide (II; R = CH_2Ph). Similarly, interaction of this chloride with the unsymmetrical

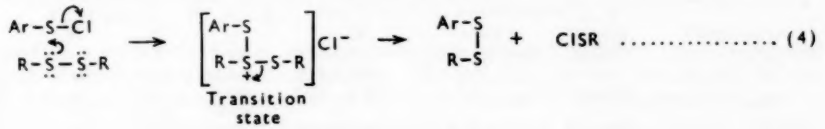
$$\underset{(I)}{ArSCl} + \underset{(III)}{RS{\cdot}SAr} \rightleftharpoons \underset{(V)}{ArS{\cdot}SAr} + \underset{(IV)}{RSCl} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

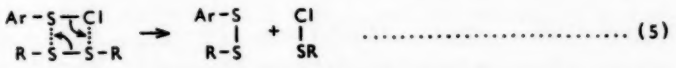
$$\underset{(I)}{ArSCl} + \underset{(III)}{RS{\cdot}SAr} \rightleftharpoons \underset{(III)}{ArS{\cdot}SR} + \underset{(I)}{ArSCl} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

disulphides (III; Ar = 2 : 4-dinitrophenyl, R = CH_2Ph or *p*-tolyl) in anhydrous acetic acid failed to give any of the highly insoluble disulphide (V; Ar = 2 : 4-dinitrophenyl). Special effects must be operative, therefore, in these systems, leading to a specific orientation of S–S cleavage as in reaction (3), which perpetuates the production of the unsymmetrical compound.

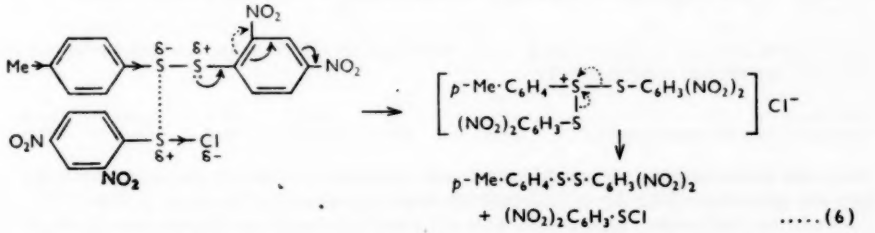
The present results, particularly the dependence of rate on the polarity of solvent, suggest that the exchange proceeds as in scheme (4), where considerable charge separation occurs in the transition state, rather than by a concerted process (5). The attacking agent is probably a polarised ArS–Cl molecule, as in (4), rather than the arenesulphenium

ion, $Ar{-}S^+$, since there is no evidence for ionisation in acetic acid solution of the arenesulphenyl chlorides studied in this work.[1] The non-occurrence of reaction (2*a*) in the systems now described is in agreement with the proposed mechanism, since electronic





factors would operate during the reaction of the unsymmetrical disulphide (III) with the sulphenyl halide (I) to favour heterolysis of the S–S bond in a preferred direction, leading to regeneration of the same disulphide (III) (reaction 3), *e.g.*, scheme 6.



The present reaction, as represented by scheme (4), bears a formal resemblance to the well-founded mechanism for the addition of sulphenyl halides to olefins,[2,3] and affords a further example of the infrequently observed heterolysis of S–S bonds by an *electrophilic* reagent.[4]

Experimental.—Materials. Unsymmetrical disulphides were prepared from the appropriate thiol and arenesulphenyl chloride in anhydrous ether [5] and recrystallised from ethanol, except for *4-carboxy-2-nitrophenyl phenyl disulphide* which was obtained as yellow needles (from carbon tetrachloride), m. p. 171·5—172·5° (Found: C, 50·5; H, 3·1; S, 20·7. $C_{13}H_9O_4NS_2$ equ ires C, 50·8; H, 3·0; S, 20·9%).

Reaction of arenesulphenyl chlorides with symmetrical disulphides. (1) In acetic acid. (i) The sulphenyl chloride [6,7] (1 millimole) and the disulphide (1 millimole) in " Reagent-grade " acetic acid (10 ml.) were kept at room temperature in the dark. The unsymmetrical disulphide usually separated out in 3—5 days and was freed from minor amounts of the hydrolysis products of the sulphenyl chloride [mainly the diaryl disulphide (V; Ar = 2 : 4-dinitrophenyl or 4-carboxy-2-nitrophenyl)] by extraction with hot ethanol and crystallisation from the same solvent. Examples are given in the Table. No diaryl disulphide (V) was formed when anhydrous acetic acid was used as solvent.

(ii) Reaction of the chloride (I; Ar = 2 : 4-dinitrophenyl) (2 mol.) with the disulphide (II; R = CH_2Ph) (1 mol.) in anhydrous acetic acid, as in (i) above, gave the product (III; Ar = 2 : 4-dinitrophenyl, R = CH_2Ph) but no product (V; Ar = 2 : 4-dinitrophenyl) even after 3 months. Similar results were obtained when using ether as solvent.

(iii) The disulphide (II; R = *p*-tolyl) (0·0025 mole) was dissolved in a 0·1M-solution (25·0 ml.) of the chloride (I; Ar = 2 : 4-dinitrophenyl) in anhydrous acetic acid, and reaction

[1] Kharasch, Buess, and King, *J. Amer. Chem. Soc.*, 1953, **75**, 6035, and references cited therein.
[2] Kharasch and Buess, *ibid.*, 1949, **71**, 2724.
[3] Orr and Kharasch, *ibid.*, 1956, **78**, 1201.
[4] Bateman, Moore, and Porter, *J.*, 1958, 2866, and references therein.
[5] Böhme and Stachel, *Z. analyt. Chem.*, 1956, **154**, 27.
[6] Kharasch, Gleason, and Buess, *J. Amer. Chem. Soc.*, 1950, **72**, 1796.
[7] Havlik and Kharasch, *ibid.*, 1955, **77**, 1150.

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Reaction of arenesulphenyl chlorides (1 *mol.*) *with symmetrical disulphides* (1 *mol.*) *in acetic acid at* ca. 20°.

Reactants		Disulphide product, ArS·SR					
					Found (%) [g]		
Ar in ArSCl	R in RS·SR	Yield [a]	M. p.[f]	C	H	N	S
$(NO_2)_2C_6H_3$	Benzyl	68% in 3 days	111—112°	48·3	3·0	—	19·8, 20·0
			(111—112)	(48·4)	(3·1)	(8·7)	(19·9)
,, ...	Phenyl	*b*	84·2—85·2	46·8	2·9	—	20·9
			c	(46·8)	(2·6)	(9·1	(20·8)
,, ...	*p*-Tolyl	*d*	111—112	48·6	3·2	—	20·2
			(111—113)	(48·4)	(3·1)	(8·7)	(19·9)
$NO_2{\cdot}C_6H_3(CO_2H)$ ...	Phenyl	18% in 3 days	172—173	50·7	3·2	—	20·5
			(171·5—172·5)	(50·8)	(3·0)	(4·6)	(20·9)
,,	*n*-Butyl	25% in 5 days	128·5—130	46·0	4·8	4·5	22·4
			e	(46·0)	(4·6)	(4·9)	(22·3)

[a] These represent the amounts precipitated after the stated times and not the maximum yields obtainable. [b] Was not precipitated, but a yield of 16% was obtained by working up the reaction product. [c] Ref. 5 gives m. p. 86°. [d] Was not precipitated; 22% was obtained on working up after 7 days. [e] New compound. [f] Mixed m. p. in parentheses. [g] Calc. figures in parentheses.

was effected as in (i). Aliquot parts were withdrawn at intervals and the sulphenyl chloride contents determined iodometrically: [8]

Time (hr.)	0	16·5	23·0	42·5	138·0
Sulphenyl chloride remaining (%)	100	95·4	95·2	95·8	92·9

The solid obtained from the combined titrated solutions was recrystallised from ethanol, to give the disulphide (III; Ar = 2 : 4-dinitrophenyl, R = *p*-tolyl) (11%), m. p. 111—112°.

(2) In other solvents. (i) Reaction of the chloride (I; Ar = 2 : 4-dinitrophenyl) (1 millimole) with dibenzyl disulphide (1 millimole) in anhydrous ether (10 ml.) for 5 days at room temperature in the dark gave the product (III; Ar = 2 : 4-dinitrophenyl, R = CH_2Ph) (45%), m. p. 110·5—112° (Found: C, 48·5; H, 3·2; S, 19·9%). (ii) No unsymmetrical disulphide separated when a carbon tetrachloride solution of the same reactants as in (i) was kept for 14 days at room temperature; removal of the solvent at 30° and fractional crystallisation of the product gave unchanged reactants (II; R = CH_2Ph) and (III; Ar = 2 : 4-dinitrophenyl, R = CH_2Ph) (9%), m. p. 109—110·5° (Found: C, 48·6; H, 3·5; N, 8·7, 8·8%). (iii) The same disulphide (III) (27%) was obtained by heating the reactants in xylene on the steam-bath for 1 hr. (iv) No disulphide (III; Ar = 2 : 4-dinitrophenyl, R = *p*-tolyl) was isolated from a mixture of the chloride (I; Ar = 2 : 4-dinitrophenyl) (2·5 millimole) and di-*p*-tolyl disulphide (2·5 millimole) in anhydrous ether (50 ml.) after 18 days at room temperature. That insignificant reaction had occurred was confirmed by addition of aniline (5 millimole) in ether (5 ml.); the disulphide (II; R = *p*-tolyl) (2·45 millimole, 98%) was recovered and 2 : 4-dinitrobenzenesulphenanilide (0·75 millimole, 30%) was isolated; this had 141·5—143° (lit.,[9] m. p. 142·5—143°) (Found: C, 49·7; H, 3·3; S, 11·0. Calc. for $C_{12}H_9O_4N_3S$: C, 49·5; H, 3·1; S, 11·0%).

Action of the chloride (I; Ar = 2 : 4-*dinitrophenyl*) *on unsymmetrical disulphides.* When equimolar amounts of the sulphenyl chloride and the disulphide (III; Ar = 2 : 4-dinitrophenyl, R = CH_2Ph or *p*-tolyl) were dissolved in anhydrous acetic acid and the mixture was kept at room temperature none of the highly insoluble compound (V; Ar = 2 : 4-dinitrophenyl) separated, even after several months.

THE BRITISH RUBBER PRODUCERS' RESEARCH ASSOCIATION,
48–56 TEWIN ROAD, WELWYN GARDEN CITY, HERTS.

[*Received, March 24th,* 1958.]

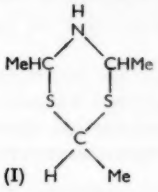
[8] Kharasch and Wald, *Analyt. Chem.*, 1955, **27**, 996.
[9] Billman, Garrison, Anderson, and Wolnak, *J. Amer. Chem. Soc.*, 1941, **63**, 1920.

585. *The Basicity of Dihydrothia-azetidines, Dihydrodithiazines, and Tetrahydrothiadiazines.*

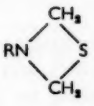
By D. J. Collins and J. Graymore.

Thialdine (I) is a very weak base, forming salts only with strong acids, these salts being extensively hydrolysed in aqueous solutions. The pK_a of thialdine was found, by the method of Bennett, Brooks, and Glasstone,[1] to be 2·85 at 25° in 30% aqueous ethanol.

The pK_a's of 3-*cyclo*hexyl-2 : 3-dihydro-1-thia-3-azetidine (II; R = C_6H_{11}), 5-*cyclo*hexyl-5 : 6-dihydro-1 : 3 : 5-dithiazine (III; R = C_6H_{11}), and the first pK_a of 3 : 5-di-*cyclo*hexyltetrahydro-1 : 3 : 5-thiadiazine, (IV; R = C_6H_{11}) were similarly found in 95% aqueous ethanol at 25° to be 2·6, 2·8, and 2·0 respectively. The pK_a of thialdine was also measured in 95% aqueous ethanol and found to be 2·7 at 25°. Change of solvent therefore appears to have little effect on the values obtained.



(I)



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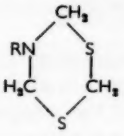
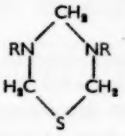


(III)



(IV)

The weak basicity of these compounds must presumably be attributed to inductive effects. There appears to be little experimental indication of the base-weakening effect of an α-sulphur substituent, probably owing to the ease with which compounds of this type undergo fission. In this connexion we found that the energy of activation for the quaternisation of diethylaminomethyl ethyl sulphide in nitrobenzene is 11,400 cal. mole^{-1}, which may be compared with that[2] (9700 cals. mole^{-1}) for the similar quaternisation of triethylamine.

The quaternisation of the cyclic bases with methyl iodide in nitrobenzene slowly proceeded to equilibria.

Plymouth and Devonport Technical College, Plymouth. [*Received, July 16th*, 1957.]

[1] Bennett, Brooks, and Glasstone, *J.*, 1935, 1821.
[2] Hinshelwood and Laidler, *J.*, 1938, 848.

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586. *Action of Organomagnesium Halides on Diaroyl Disulphides.*

By Mohamed A. Elkaschef and Michael H. Nosseir.

In their reaction with organomagnesium compounds diaryl disulphides were found by Wuyts[1] to behave as esters of hydrogen disulphide and undergo fission, RS·SR + R′·MgBr ⟶ RR′S + RS·MgBr, with final production of mixed sulphides and thiophenols. Disulphides were found by Schönberg *et al.*[2] to behave similarly towards phenyl-lithium. Gilman *et al.*[3] report that four mols. of phenylmagnesium bromide with one of ethyl thionbenzoate give benzophenone and two unidentified sulphur-containing compounds, or with one mol. of ethyl dithiobenzoate give a magnesium complex which, when treated with benzoyl chloride, gives triphenylmethyl thiobenzoate, proving that the phenyl group of the Grignard reagent adds to the carbon atom of the thiocarbonyl group and the MgBr to the sulphur, as is to be expected.

[1] Wuyts, *Bull. Soc. chim. France*, 1906, **35**, 166.
[2] Schönberg, Stephenson, Kaltschmitt, Petersen, and Schulten, *Ber.*, 1933, **66**, 237.
[3] Gilman, Robinson, and Beaber, *J. Amer. Chem. Soc.*, 1926, **48**, 2715.

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Hepworth and Clapham,[4] using aryl- or alkyl-magnesium halides and ethyl thiobenzoate, thiocarbonate, and thioacetate, obtained tertiary alcohols and the thiol from which the thio-ester was derived. On the other hand, aroyl peroxides, which may be regarded as esters of hydrogen peroxide, were found by Gilman and Adams [5] to undergo fission, as in the case of disulphides, and in presence of phenylmagnesium bromide reaction goes further and affords triarylmethanol and phenol.

The present work concerns the action of arylmagnesium halides on diaroyl disulphides. When three mols. of phenylmagnesium bromide are added to one of dibenzoyl disulphide or of di-*p*-anisoyl disulphide and the magnesium complex is decomposed with sulphuric acid triphenylmethyl thiobenzoate and *p*-methoxyphenyldiphenylmethyl *p*-thioanisate respectively are obtained; when the decomposition is carried out with ammonium chloride the first disulphide gives triphenylmethanol and thiobenzoic acid, and the second gives phenyl *p*-thioanisate. *p*-Methoxyphenyl- or naphthyl-magnesium bromide with dibenzoyl disulphide gives respectively *p*-methoxyphenyl or naphthyl thiobenzoate, whichever method of decomposition is used. Use of six mols. of phenylmagnesium bromide and dibenzoyl disulphide affords triphenylmethanol, whilst two mols. give an unidentified unstable oil.

On decomposition of the magnesium complexes hydrogen sulphide was evolved. The odour of thiophenol was observed in almost all cases and thiophenol was proved to the present after decomposition of the complex leading to triphenylmethyl thiobenzoate.[6] These facts may explain the non-appearance of one of the sulphur atoms in the final products.

Experimental.—Action of phenylmagnesium bromide on dibenzoyl disulphide. (a) **3** *mols. of bromide and* **1** *of disulphide.* (i) A Grignard solution from magnesium (0·72 g.), bromobenzene (3·2 c.c.), and ether (40 c.c.) was cooled to 0° and added to an ice-cold solution of dibenzoyl disulphide (2·74 g.) in benzene (70 c.c.). The mixture was refluxed for 2 hr., then kept overnight and poured into water (150 c.c.), ice (100 g.), and concentrated sulphuric acid (2·5 c.c.). Hydrogen sulphide was evolved and the smell of thiophenol was prominent. The organic layer was separated, the aqueous layer was extracted with ether, and the organic liquids were united, washed with water, dried (Na_2SO_4), and evaporated. The resultant oil crystallised on addition of light petroleum (b. p. 60—90°) and cooling. The solid triphenylmethyl thiobenzoate, recrystallised from light petroleum (b. p. 100—120°), had m. p. and mixed m. p. (cf. ref. 3) 188° and gave an orange colour in concentrated sulphuric acid (Found: C, 81·9; H, 5·2; S, 8·2. Calc. for $C_{26}H_{20}O_2S$: C, 82·1; H, 5·3; S, 8·4%).

To triphenylmethyl thiobenzoate (0·4 g.) in boiling acetic acid (20 c.c.) containing 1 c.c. of concentrated hydrochloric acid, zinc powder (activated with copper sulphate) (0·7 g.) was added, and the whole was refluxed for 6 hr. After cooling, the mixture was poured into water. Isolation with ether afforded triphenylmethane, m. p. and mixed m. p. (cf. ref. 7) 91°, and benzoic acid, m. p. and mixed m. p. 121°.

(ii) After a similar reaction the mixture was decomposed with ammonium chloride solution and ice. The organic layers yielded triphenylmethanol (1·2 g.), m. p. and mixed m. p. (cf. ref. 8) 163° from light petroleum (b. p. 60—90°). The aqueous layer on acidification gave thiobenzoic acid.

(b) *Six mols. of bromide and one of disulphide.* In reaction as above, with decomposition by acid, dibenzoyl disulphide (2·74 g.) and a Grignard reagent from bromobenzene (6·4 c.c.) gave triphenylmethanol (1·2 g.), m. p. and mixed m. p. 163°.

(c) *Two mols. of bromide and one of disulphide.* This reaction gave an unidentified red oil that decomposed spontaneously with evolution of hydrogen sulphide.

Action of p-*methoxyphenylmagnesium bromide* (3 *mols.*) *on dibenzoyl disulphide* (1 *mol.*). Dibenzoyl disulphide (2·7 g.) and a Grignard reagent from *p*-bromoanisole (5·6 g.), in a reaction as above, with refluxing for 3·5 hr. and decomposition with either sulphuric acid or ammonium

[4] Hepworth and Clapham, *J.*, 1921, **119**, 188.
[5] Gilman and Adams, *J. Amer. Chem. Soc.*, 1926, **47**, 2816.
[6] Rheinbolt's test for thiophenol, *Ber.*, 1927, **60**, 184.
[7] Gomberg, *Ber.*, 1903, **36**, 383.
[8] Acree, *Ber.*, 1904, **37**, 2755.

chloride, gave p-*methoxyphenyl thiobenzoate* from the organic layers as an oil which solidified under ethanol and, recrystallised therefrom (yield, 1·5 g.), had m. p. 102° and dissolved in concentrated sulphuric acid with a greenish yellow colour (Found: C, 68·7; H, 4·9; S, 13·0. $C_{14}H_{12}O_2S$ requires C, 68·8; H, 4·9; S, 13·1%).

Action of α-naphthylmagnesium bromide (3 *mols.*) *on dibenzoyl disulphide* (1 *mol.*). This reaction, with 3 hours' boiling and decomposition by either method, gave α-naphthyl thiobenzoate, m. p. 119° (cf. ref. 9) (from light petroleum), giving a green colour in sulphuric acid (Found: C, 77·1; H, 4·8; S, 11·8. Calc. for $C_{17}H_{12}OS$: C, 77·2; H, 4·5; S, 12·1%).

Action of phenylmagnesium bromide (3 *mols.*) *on di-p-anisoyl disulphide* (1 *mol.*). (i) Phenylmagnesium bromide (from 3·2 c.c. of bromobenzene) and di-*p*-anisoyl disulphide (3·3 g.), in a reaction as above, with refluxing for 5·5 hr. and decomposition with acid, gave p-*methoxyphenyldiphenylmethyl* p-*thioanisate* (2·8 g.), m. p. 178° [from light petroleum (b. p. 100—120°)], giving an orange solution in sulphuric acid (Found: C, 76·6; H, 5·4; S, 7·1. $C_{28}H_{24}O_3S$ requires C, 76·3; H, 5·4; S, 7·3%).

Reduction of this product as above gave *p*-anisic acid, m. p. and mixed m. p. 184°.

Boiling the ester for 1 hr. in ethanol containing concentrated hydrochloric acid (100 : 15 parts by vol.) gave *p*-anisic acid, m. p. 184°, and *p*-methoxyphenyldiphenylmethanol, m. p. and mixed m. p. (cf. ref. 10) 84° (from light petroleum–ether).

(ii) Reaction as above, but decomposition with ammonium chloride and ice, gave *phenyl* p-*thioanisate*, m. p. 99° [from light petroleum (b. p. 60—90°)] (yield 0·8 g.) (Found: C, 69·1; H, 4·9; S, 13·0. $C_{14}H_{12}O_2S$ requires C, 68·8; H, 4·9; S, 13·0%).

The same ester was obtained (m. p. and mixed m. p. 99°) by refluxing equimolecular amounts of *p*-anisoyl chloride with thiophenol.

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DOKKY, GUIZEH, EGYPT. [*Received, September 16th*, 1957.]

[9] Taboury, *Compt. rend.*, 1904, **188**, 983.
[10] Kovache, *Ann. Chim.* (*France*), 1918, **10**, 200.

587. *Back-co-ordination from Oxygen to Boron in Organoboron Compounds.*

By E. W. ABEL, W. GERRARD, M. F. LAPPERT, and R. SHAFFERMAN.

SOME interest attaches to co-ordination at a tervalent boron atom in organoboron compounds; for it is hoped that intramolecular or intermolecular co-ordination might be harnessed, not only to eliminate ease of hydrolysis or of oxidation, but also to encourage cross-linking in the development of polymers.

In an investigation into factors influencing the co-ordination of amines to boron attached to oxygen, the base was added to the boron compound in a solvent. When there was no precipitate, heat of mixing indicated association, whereas a precipitated complex is described as stable if it remained after being for several hours at 20°/20 mm., and as unstable if under these conditions dissociation occurred. Results are recorded in Table 1.

In the trialkyl borates, back-co-ordination from three atoms of oxygen satisfies acceptor properties of boron, and repels outside donor molecules. Even when R = $CCl_3{\cdot}CH_2$, the inductive effect of nine atoms of chlorine does not reduce back-co-ordination sufficiently (possible *F*-strain being ignored), although the effect of nine atoms of fluorine does so. When R = Ph in any of the esters, back-co-ordination is very effectively compensated, presumably by an *M*-effect, although even then for the borates, complex formation can be hindered by *F*-strain due to *ortho*- or di-*ortho*-substitution in the ring. Phenyl attached to boron, as in the esters, $Ph{\cdot}B(OR)_2$, compensates back-co-ordination from two atoms of oxygen, by a mechanism which is not clear unless polarisability of phenyl allows co-ordination to occur. Results for the esters of diphenylboronous acid are in accordance with these comments. When *n*-butyl, instead of phenyl, is attached to boron [$BuB(OR)_2$], back-co-ordination from two atoms of oxygen is sufficient to impede

complex-formation with an external base, the $+I$-effect of the alkyl group attached to boron being insufficient itself to impede complex formation, as is clear from the fact that when two butyl groups are directly attached to boron [$Bu_2B{\cdot}OR$], evidence of complex-formation is found.

When the chain of the alkoxyl group is lengthened, Me to Et to Bu^n, decrease in stability of the corresponding complex is noticeable.

Table 2 gives results for a number of other nitrogen donor molecules, to show that overlying the factors mentioned there are steric factors related to the base which shift the stability of the complexes in one direction without altering the relation discussed.

TABLE 1. 1 : 1 *Complex formation with pyridine.*

R	$B(OR)_3$	$Ph{\cdot}B(OR)_2$	$Bu^n{\cdot}B(OR)_2$	$Ph_2B{\cdot}OR$	$Bu^n_2B{\cdot}OR$
Me	None [1]	Stable	Assocn.	Stable	Unstable
Et	—	Unstable	—	Stable	Assocn.
$CCl_3{\cdot}CH_2$	None [2]	Stable [2]	—	—	—
$CF_3{\cdot}CH_2$	Stable	—	—	Stable	Stable
Pr^n	—	—	—	Stable	—
Bu^n	None	—	None [2]	Assocn.	—
Ph	Stable	Stable [4]	Stable	Stable	Stable
$2\text{-}C_6H_4Y$	Unstable [3]	—	—	—	—
$2:6\text{-}C_6H_4Y_2$	None [3]	—	—	—	—

Y = Me, MeO, or Cl. Y′ = NO_2 or I.

TABLE 2. *Boron ester–amine co-ordination.*

	NH_3	$Et{\cdot}NH_2$	Et_2NH	Et_3N
$B(OPh)_3$ [3]	Stable	Stable	Unstable	Assocn.
$Ph{\cdot}B(OBu^n)_2$	Stable [5]	Assocn.	No assocn.	No assocn.
$Bu^n{\cdot}B(OMe)_2$	Unstable	No assocn.	No assocn.	No assocn.
$Ph_2B{\cdot}OBu^n$	Stable	Unstable	Assocn.	No assocn.
$Bu^n_2B{\cdot}OMe$	Unstable	Unstable	No assocn.	No assocn.
$Bu^n_2B{\cdot}OEt$	Unstable	Assocn.	No assocn.	No assocn.

TABLE 3. *Characterisation of complexes.*

		Found (%)		Required (%)	
Complex	M. p.*	Amine	B	Amine	B
$B(O{\cdot}CH_2{\cdot}CF_3)_3,NC_5H_5$	48°	21·1	2·9	20·4	2·8
$Ph{\cdot}B(OMe)_2,NC_5H_5$	31	34·9	4·8	34·6	4·7
$Bu^n{\cdot}B(OPh)_2,NC_5H_5$	66—70	23·5	3·1	23·7	3·3
$Ph_2B{\cdot}OMe,NC_5H_5$	78—80	28·5	3·8	28·8	3·9
$Ph_2B{\cdot}OEt,NC_5H_5$	80—82	27·6	3·5	27·4	3·7
$Ph_2B{\cdot}OPr^n,NC_5H_5$	57	26·5	3·5	26·1	3·6
$Ph_2B{\cdot}O{\cdot}CH_2{\cdot}CF_3,NC_5H_5$ †	97	21·9	—	23·1	—
$Ph_2B{\cdot}OPh,NC_5H_5$	—	23·6	3·4	23·2	3·2
$Bu^n_2B{\cdot}O{\cdot}CH_2{\cdot}CF_2,NC_5H_5$	*ca.* 4	25·8	3·3	26·1	3·6
$Bu^n_2B{\cdot}OPh,NC_5H_5$	56—57	26·8	3·3	26·7	3·6
$Ph_2B{\cdot}OBu^n,NH_3$	71—74	6·3	4·1	6·5	4·3
$Ph_2B{\cdot}OBu^n,Et{\cdot}NH_2$	61—63	15·7	3·8	15·9	3·8

* In sealed tubes. † Found: C, 66·9; H, 5·2. $C_{19}H_{17}ONF_3B$ requires C, 66·5; H, 5·0%.

Experimental.—Tris-2 : 2 : 2-trifluoroethyl borate (70%), b. p. 43°/60 mm., n_D^{20} 1·297 (Found: C, 23·6; H, 2·6; B, 3·55. $C_6H_6O_3F_9B$ requires C, 23·4; H, 2·0; B, 3·52%), was obtained by slow addition of 2 : 2 : 2-trifluoroethanol (3 mols.) in *n*-pentane to boron trichloride (1 mol.) in *n*-pentane at −80°, hydrogen chloride and solvent being then removed at 20°/100 mm.

2 : 2 : 2-Trifluoroethyl diphenylboronite (73%), b. p. 90°/0·2 mm., n_D^{20} 1·5190, d_4^{20} 1·1706 (Found: C, 63·8; H, 4·6; B, 4·12. $C_{14}H_{12}OF_3B$ requires C, 63·9; H, 5·9; B, 4·10%), was similarly obtained by equimolar interaction of diphenylboron chloride [6] and the alcohol.

[1] Venkataramaraj Urs and Gould, *J. Amer. Chem. Soc.*, 1952, **74**, 2948.
[2] Brindley, Gerrard, and Lappert, *J.*, 1956, 1540.
[3] Colclough, Gerrard, and Lappert, *J.*, 1955, 907; 1956, 3006.
[4] Dandegaonker, Gerrard, and Lappert, *J.*, 1957, 2872.
[5] Letsinger and Skoog, *J. Amer. Chem. Soc.*, 1955, **77**, 2491.
[6] Abel, Dandegaonker, Gerrard, and Lappert, *J.*, 1956, 4697.

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References to the preparation of other esters are: phenylboronates, $Ph{\cdot}B(OR)_2$, R = Me,[4] Et,[7] Ph [4]; *n*-butylboronates, $Bu^n{\cdot}B(OR)_2$, R = Me, Ph [8]; diphenylboronites, $Ph_2B{\cdot}OR$,[9] and di-*n*-butylboronites, $Bu^n_2B{\cdot}OR$, R = Me,[8] Et,[8] $F_3C{\cdot}CH_2$,[8] Ph.[10]

Complexes isolated are listed in Table 3.

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[7] Brindley, Gerrard, and Lappert, *J.*, 1955, 2956.
[8] Gerrard, Lappert, and Shafferman, unpublished work.
[9] Abel, Gerrard, and Lappert, *J.*, 1957, 112.
[10] Gerrard, Lappert, and Shafferman, *J.*, 1957, 3828.

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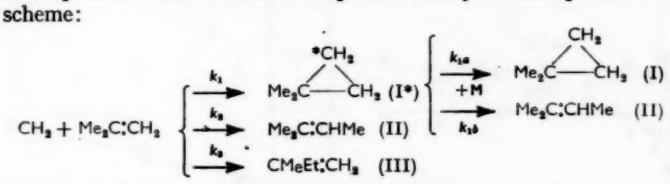
588. *Reactions of Methylene with* iso*Butene.*

By J. H. KNOX, A. F. TROTMAN-DICKENSON, and C. H. J. WELLS.

THE reactions of methylene with *iso*butene have been studied by photolysing keten in the presence of the olefin (ratio 1 : 2·8) in a Pyrex vessel with light from a medium-pressure mercury arc. The products were analysed by gas chromatography and identified by their infrared spectra. The formation of products may be interpreted in terms of the following scheme:



The variation of the yields of (I), (II), and (III) with pressure, shown in Fig. 1 for 20°, indicate that at pressures above about 4 cm. effectively all the (I*) molecules are deactivated by collision, *i.e.*, $k_{1a}[M] \gg k_{1b}$. At the higher pressures, therefore, the values of the relative yields give the ratios of the rate constants k_1, k_2, and k_3. The effect of temperature on the high-pressure ratios is shown in Fig. 2. The straight lines have the equations:

$$k_1/k_2 = 6{\cdot}0 \exp [+ 180 \text{ cal. mole}^{-1}/RT]$$
$$k_3/k_2 = 1{\cdot}2 \exp [+ 430 \text{ cal. mole}^{-1}/RT]$$

Addition to the double bond is several times more rapid than insertion into the C–H bonds. This is in agreement with Frey [1] who showed that for ethylene $k_1/k_2 = 1{\cdot}6$, after allowance for 4 ethylenic bonds in ethylene and only two in *iso*butene. Skell and Woodworth's results [2] on the reaction of methylene with *cis*-but-2-ene and Skell and Garner's [3] on the reactions of CBr_2 with olefins in general confirm the conclusion.

The small activation-energy differences are of the same order as those previously found for insertion of CH_2 into saturated hydrocarbons.[4] They likewise fall in an unexpected order in that $E_{CH_3} > E_{C=C} > E_{CH_2}$. However, their absolute values are probably low and are likely to be determined by steric requirements rather than by the strengths of the bonds broken or formed. The *A* factor ratios can be expressed in terms of the rates of attack on individual bonds as

$$A_{C=C} : A_{CH_3} : A_{CH_2} = 12 : 1{\cdot}00 : 0{\cdot}4$$

showing that the high reactivity of the double bond is due to a high entropy of activation, not to a low energy of activation. Skell and Woodworth's finding [2] that the

[1] Frey, *J. Amer. Chem. Soc.*, 1957, **79**, 1259.
[2] Skell and Woodworth, *ibid.*, 1956, **78**, 4496.
[3] Skell and Garner, *ibid.*, pp. 3409, 5431.
[4] Knox and Trotman-Dickenson, *Chem. and Ind.*, 1957, 731.

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addition of CH_2 to *cis*-but-2-ene is stereospecific rules out the possibility that this high entropy is due to free rotation in the activated complex. Skell and Garner's results [3] on the reactions of CBr_2 show that its reactions are much more selective than those of methylene. Addition to *iso*butene is, for example, some 14 times as fast as the addition to hex-1-ene, whereas preliminary results with methylene indicate that its addition to *iso*butene and pent-1-ene occur at roughly the same rate.

At low pressures, as seen from Fig. 1, the ratios I/II and III/II fall as the pressure is reduced while (I + II)/III remains constant. Compounds (I) and (II) are, therefore, alternative final products, the latter being increasingly favoured at lower pressures. This is in full accord with the scheme outlined above, where activated 1 : 1-dimethyl*cyclo*propane

FIG. 1.

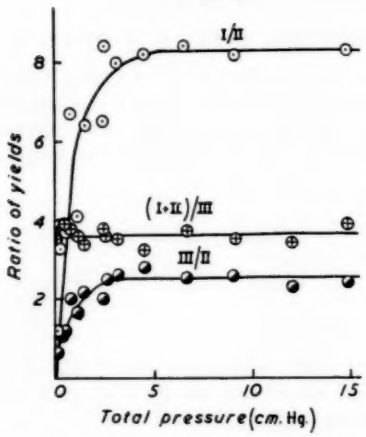
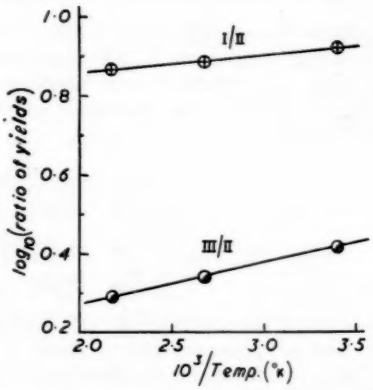


FIG. 2.



either isomerises [to (II)] or is stabilised by collision. The limiting pressure for stabilisation (about 4 cm.) may be compared with the corresponding pressure for activated *cyclo*propane [5] (about 200 cm.) and methyl*cyclo*propane [6] (about 40 cm.) formed by similar reactions of methylene with ethylene and propene. The larger number of degrees of freedom in the more complex activated molecules account for their greater lifetimes.

The isomerisation of (I*) might yield either 2-methylbut-2-ene (II) or 3-methylbut-1-ene (IV). Small quantities of the latter which has a boiling point close to that of the cyclic compound (I) might not have been detected on the chromatograms, and since the infrared identification was carried out with a sample from a high-pressure experiment, there is no direct analytical evidence that the but-1-ene was not formed at low pressures. However, the yield of (I + II) closely approaches zero at low pressures and so the percentage of the but-1-ene (IV) which could have been included in the analysis as dimethyl*cyclo*propane (I) must be low. Furthermore, the standard free-energy change (ΔF°) for the conversion of (II) into (IV) is $\Delta F^\circ = +3{\cdot}61$ kcal. mole^{-1} and if the isomerisation yields the methylbutenes (II) and (IV) in equilibrium proportions only $2{\cdot}4 \times 10^{-3}$ of the product will be the latter.

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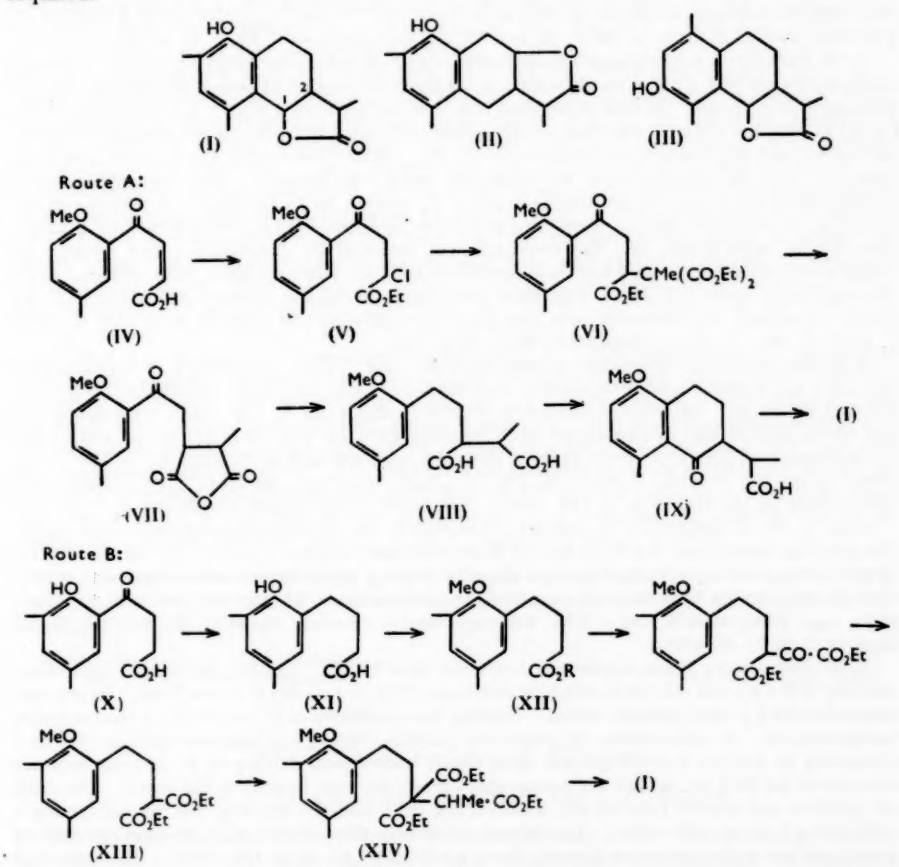
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF EDINBURGH. [*Received, March* 19*th*, 1958.]

[5] Frey and Kistiakowsky, *J. Amer. Chem. Soc.*, 1957, **79**, 6373.
[6] Knox and Trotman-Dickenson, *Chem. and Ind.*, 1957, 1039.

589. *Attempts to Synthesise* α-(1 : 2 : 3 : 4-*Tetrahydro*-1 : 5-*dihydroxy*-6 : 8-*dimethyl*-2-*naphthyl*)*propionic Lactone.*

By Wesley Cocker, T. B. H. McMurry, (Mrs.) L. Mabrouk, and W. R. N. Williamson.

In attempts to synthesise the lactone (I), which at one time was considered to be desmotropo-ψ-santonin,[1] two reaction routes, shown below, were employed. Neither was successful, but a number of intermediates are now described. Since it is probable [2] that desmotropo-ψ-santonin has structure (II), other lines of approach to its synthesis are required.



Route A is similar to that employed by Clemo, Haworth, and Walton [3] for the synthesis of desmotroposantonin (III). In our synthesis it was proposed to introduce the second nuclear methyl group in the final or penultimate stage. Yields of products in the earlier stages were disappointing and the method was abandoned.

In route B, β-(2-hydroxy-3 : 5-dimethylbenzoyl)propionic acid (X), previously prepared

[1] Cocker, Cross, and Lipman, *J.*, 1949, 939; cf. Clemo and Cocker, *J.*, 1946, 30.
[2] Chopra, Cocker, Edward, McMurry, and Stuart, *J.*, 1956, 1828.
[3] Clemo, Haworth, and Walton, *J.*, 1929, 2368; 1930, 1110.

in low yield by rearrangement of *m*-4-xylyl hydrogen succinate,[4] was produced in about 60% yield by condensation of *m*-4-xylenol with succinic anhydride in presence of aluminium chloride. The corresponding butyric acid (XI) was known,[4] and its methylation to (XII; R = H) which might have been expected to be difficult owing to hindrance was satisfactorily accomplished. Thereafter yields at each stage were disappointing, and the formation of the lactone (I) by this route is unprofitable.

Experimental.—Ultraviolet measurements were made on EtOH solutions.

Ethyl α-chloro-β-(2-methoxy-5-methylbenzoyl)propionate (V). β-(2-Methoxy-5-methylbenzoyl)acrylic acid [5] (IV) (7 g.) in absolute ethanol (60 c.c.) was saturated at 0° with hydrogen chloride; a copious white solid was deposited. After 12 hr. at 0° the solid *ester* (7 g.) was collected, washed with ice-cold ethanol, dried, and crystallised from ligroin (b. p. 80—100°) from which colourless needles, m. p. 78°, were deposited. It had $\lambda_{max.}$ 2500, 3200 Å (log ε 3·88, 3·58 respectively) (Found: C, 59·7; H, 6·2. $C_{14}H_{17}O_4Cl$ requires C, 59·1; H, 6·0%).

5-(2-Methoxy-5-methylphenyl)-5-oxopentane-2 : 3-dicarboxylic anhydride (VII). Diethyl methylmalonate (6·1 g.) was slowly added to a stirred suspension of powdered sodium (1 g.) in benzene (105 c.c.), and the stirred solution was then refluxed for 1·5 hr. The chloro-ester (V) (10 g.) in benzene (10 c.c.) was then slowly added with stirring to the cooled solution of sodio-derivative, and the mixture was refluxed for 3·5 hr. Water was added, the benzene layer was separated, and the aqueous layer was extracted twice with benzene. The combined benzene extracts were dried and the benzene was removed, leaving an oil (14·4 g.). A solution of the oil (5·7 g.) in methanol (60 c.c.) containing potassium hydroxide (12 g.) was refluxed for 2·25 hr., then diluted with water, and the methanol was removed by distillation. The residue, on acidification, afforded an oil which was heated at 160° for 1 hr., giving a resin (2·5 g.). This was triturated while still warm with light petroleum, giving the required *anhydride* (0·49 g.) which crystallised from benzene–light petroleum (b. p. 60—80°) as rhombs, m. p. 149° (Found: C, 65·2; H, 6·0. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%).

α-(2-Methoxy-5-methylphenethyl)-α'-methylsuccinic acid (VIII). A mixture of amalgamated zinc (10·5 g.), concentrated hydrochloric acid (10·5 c.c.), and the above anhydride (1·5 g.) was refluxed for 26 hr. On cooling, colourless needles (0·42 g.), m. p. 143—144°, were deposited, and extraction of the mother-liquor with benzene gave an acid (0·3 g.), m. p. 125—135°. Crystallisation of the latter from benzene gave the required *acid* as rhombs, m. p. 139°, $\lambda_{max.}$ 2790 Å (log ε 3·4) (Found: C, 64·6; H, 7·0. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·1%), which were undepressed by the acid of m. p. 143—144°. The acids are dimorphic modifications.

α-(1 : 2 : 3 : 4-Tetrahydro-5-methoxy-8-methyl-1-oxo-2-naphthyl)propionic acid (IX). The previous compound (1 g.) was heated in concentrated sulphuric acid (3 c.c.) at 65—70° for 10 min., then poured on crushed ice, and the solid (0·15 g.) was collected and washed with water. Two crystallisations from benzene gave the required *tetralone* (51 mg.) as prisms, m. p. 151—152°, $\lambda_{max.}$ 2600, 3080 Å (log ε 4·15, 3·2 respectively) (Found: C, 69·1; H, 6·6. $C_{15}H_{16}O_4$ requires C, 68·7; H, 6·9%).

β-(2-Hydroxy-3 : 5-dimethylbenzoyl)propionic acid [4] (X). Finely powdered aluminium chloride (129·5 g.) was stirred in ethylene dichloride (200 c.c.) cooled in an ice-bath, and succinic anhydride (59 g.) was gradually added. Stirring was continued at 0° for 0·5 hr., a clear solution being obtained. A cold solution of aluminium chloride (64·75 g.) in ethylene chloride (150 c.c.) containing 2 : 4-xylen-1-ol (61 g.) was then slowly added with stirring at 0° and the mixture was stirred for 22·5 hr., whilst the temperature gradually rose to that of the room. The dark red solution was poured into ice and hydrochloric acid, and the mixture was filtered, giving a solid (4·4 g.), m. p. 125—135°. The organic layer was then shaken with an equal volume of water, and the white slurry was filtered, giving a solid (55·7 g.), m. p. 144—147°. The combined solids were triturated with hot water to give the keto-acid (57 g.), m. p. 144—147° undepressed by a sample, m. p. 147—148°, prepared by the method of Cocker, Fateen, and Lipman.[4] A further quantity of the acid (11 g.; m. p. 144—147°) was obtained as follows. The ethylene dichloride–water filtrate was treated with sodium hydrogen carbonate and distilled in steam to remove solvent, and the residue acidified. The solid product was then crystallised from benzene (charcoal). The *S-benzylthiuronium salt* formed needles (from alcohol–water), m. p.

[4] Cocker, Fateen, and Lipman, *J.*, 1951, 929.
[5] Dave and Nargund, *J. Univ. Bombay*, 1938, **7**, 191; cf. "Organic Reactions," J. Wiley and Sons, New York, 1949, Vol. V, p. 286.

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151° (Found: C, 61·0; H, 6·1. $C_{20}H_{24}O_4N_2S$ requires C, 61·8; H, 6·2%), and the *ethyl ester* needles (from ethanol), m. p. 67° (Found: C, 67·4; H, 7·3. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

γ-(2-Hydroxy-3 : 5-dimethylphenyl)butyric acid. This acid was prepared as described by Cocker, Fateen, and Lipman.[4] Its *methyl ester* formed needles (from light petroleum), m. p. 55° (Found: C, 69·8; H, 8·0. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·1%).

γ-(2-Methoxy-3 : 5-dimethylphenyl)butyric acid (XII; R = H). The hydroxy-acid [4] (XI) (50·2 g.), in a solution of sodium hydroxide (80 g.) in water (320 c.c.), was stirred whilst dimethyl sulphate (155 g.) was added during 0·75 hr. The mixture was refluxed and stirred for 2·5 hr., then cooled, and acidified. The precipitated red oil (51·3 g.) was collected in ether and distilled, the fraction (34 g.) of b. p. 175—180°/7 mm. being collected. This *acid* solidified (m. p. 37—41°) (Found: C, 69·7; H, 8·15. $C_{13}H_{18}O_3$ requires C, 70·2; H, 8·1%); it gave an *S-benzylthiuronium* salt, plates (from water), m. p. 127° (Found: C, 65·1; H, 7·2. $C_{21}H_{28}O_3N_2S$ requires C, 64·9; H, 7·3%), and an *ethyl ester* (XII; R = Et), b. p. 150°/8 mm. (Found: C, 71·9; H, 9·1. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%).

Diethyl 2-methoxy-3 : 5-dimethylphenethylmalonate (XIII). The above ester (XII; R = Et) (32·9 g.), in diethyl oxalate (38·4 g.) and benzene (50 c.c.), cooled to 0°, was slowly added to an ice-cold solution of sodium ethoxide (from sodium, 6 g.) in the minimum quantity of ethanol. After 18 hr. the pink solution was added to ice and hydrochloric acid, and the benzene layer was separated. The aqueous layer was exhaustively extracted with ether, the combined organic extracts were dried, and the solvents were removed. The remaining red oil (46 g.) was heated with powdered glass (50 g.) at 150—170° for 9 hr., then distilled, a fraction (26·7 g.) of b. p. 146—160°/7 mm. being collected. Several distillations failed to narrow the boiling range, but a fraction collected at 168°/4·5 mm. was used for analysis and was the required *ester* (XIII) (Found: C, 67·6; H, 8·5. $C_{18}H_{26}O_5$ requires C, 67·1; H, 8·1%). The *diamide* crystallised as needles (from methanol), m. p. 192—193° (Found: C, 63·8; H, 7·9; N, 11·1. $C_{14}H_{20}O_3N_2$ requires C, 63·6; H, 7·6; N, 10·6%).

Triethyl 5-(2-methoxy-3 : 5-dimethylphenyl)pentane-2 : 3 : 3-tricarboxylate (XIV). Potassium (0·97 g.) was dissolved in ethanol, and the solvent was then removed until a white flocculent precipitate appeared. The malonic ester (XIII) (8·6 g.) was then added with shaking and the remainder of the ethanol was removed, leaving a red jelly. Ethyl α-bromopropionate (5 c.c.) was then added slowly with shaking, and the mixture was heated at 100° for 3·5 hr., and kept at room temperature for 36 hr. The product was dissolved in ether and filtered to remove potassium bromide. Distillation of the ethereal extract gave a colourless oil (6·1 g.), b. p. 187—200°/6 mm. A specimen of the *tricarboxylic ester* collected for analysis had b. p. 200°/6 mm. (Found: C, 65·15; H, 8·3. $C_{23}H_{34}O_7$ requires C, 65·4; H, 8·1%).

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590. *Three Iodides of Rhenium.*

By R. D. PEACOCK, A. J. E. WELCH, and L. F. WILSON.

ALTHOUGH fluorides, chlorides, and bromides of rhenium are known, the existence of iodides has been disputed. The early claim of I. and W. Noddack that rhenium tetraiodide is formed from the elements on heating has not been substantiated,[1] and work in these laboratories shows that iodine does not combine with rhenium even at red heat. We have now successfully isolated rhenium tetraiodide by a method analogous to that used in making the corresponding osmium compound OsI_4 from osmic acid,[2] namely, the reduction of per-rhenic acid by hydriodic acid.

[1] Rulfs and Elving, *J. Amer. Chem. Soc.*, 1950, **72**, 3304.
[2] Cf. Sidgwick, "The Chemical Elements and their Compounds," Clarendon Press, Oxford, 1950, Vol. II, p. 1494.

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Per-rhenic acid is acted on by cold hydriodic acid, iodine is released, and a dark brown solution is formed. Evaporation to dryness at room temperature yields black rhenium tetraiodide, which *X*-ray photographs show to be nearly non-crystalline. At an intermediate stage in the evaporation black plate-like crystals, presumably of hydrated iodorhenic acid H_2ReI_6,nH_2O, appear. The tetraiodide is very hygroscopic and dissolves easily in water to give a brown solution which, however, soon hydrolyses, depositing hydrated rhenium dioxide, ReO_2,nH_2O. It is also soluble in acetone and ether to give dark brown solutions.

Rhenium tetraiodide is unstable; it loses iodine in a vacuum at room temperature, and when heated rapidly decomposes. Weight losses during this thermal decomposition appear to indicate two solid iodide phases, the tri-iodide, ReI_3, and the monoiodide, ReI.

Rhenium tri-iodide is a black crystalline solid obtained by heating rhenium tetraiodide in a sealed tube to 350°. Alternatively, ammonium iodorhenate $(NH_4)_2ReI_6$ is decomposed in a vacuum at 325°, and the solid residue heated with excess of iodine in a sealed tube at 200°. In both instances the superfluous iodine is dissolved in carbon tetrachloride, which leaves the insoluble rhenium tri-iodide. The tri-iodide is only slightly soluble in water (cf. RuI_3) and dilute acids; it is nearly insoluble in alcohol, acetone, and ether. Like the tetraiodide, it loses iodine slowly in a vacuum, especially when warmed.

The phase formed when the tetraiodide is heated to constant weight at 110° in a stream of nitrogen containing a little iodine is rhenium monoiodide. *X*-Ray photographs show this to have a simple cubic unit cell, with a cell edge of 9·33 Å. It recombines with iodine at 200° in a sealed tube to form the tri-iodide; when heated alone in a vacuum the ultimate product is rhenium metal.

Experimental.—Rhenium tetraiodide. Rhenium metal powder (1 g.) was dissolved in dilute hydrogen peroxide (20 vol.). The colourless solution was evaporated nearly to dryness on a steam-bath several times to remove excess of hydrogen peroxide. 15 ml. of water were added, followed by a large excess of concentrated hydriodic acid which had been freshly distilled over red phosphorus. The solution was evaporated almost to dryness in a vacuum desiccator and was allowed to stand for 3 days in a desiccator over phosphorus pentoxide and solid sodium hydroxide. (The product loses iodine progressively under a vacuum.) The black amorphous residue was *rhenium tetraiodide* (Found: Re, 27·1; I, 73·4. ReI_4 requires Re, 26·8; I, 73·2%). Its infrared spectrum showed H_2O and −OH to be absent.

Rhenium tri-iodide. Rhenium tetraiodide (0·2 g.) was heated in a sealed tube at 350° for 6 hr. After the tube was cooled and opened, excess of iodine was removed from the product by washing with carbon tetrachloride, in which the *tri-iodide* is insoluble (Found: I, 67·7. ReI_3 requires I, 67·1%). Alternatively, ammonium iodorhenate(IV) (2 g.) was heated in a vacuum at 325° for several hr.; the cold residue, which consisted essentially of impure rhenium monoiodide, was heated with excess of iodine in a sealed tube at 200°. The product, which was a mixture of tri-iodide and iodine, was washed with carbon tetrachloride or water to remove the iodine (Found: Re, 33·2; I, 66·6. ReI_3 requires Re, 32·9; I, 67·1%).

Rhenium monoiodide. Rhenium tetraiodide (0·2 g.) was heated to 110° in a stream of nitrogen in the presence of a small vapour pressure (15 mm.) of iodine for 16 hr. The product was *rhenium monoiodide* (Found: Re, 60·2; I, 39·4. ReI requires Re 59·5; I, 40·5%).

Analysis.—Iodine. Portions (40 mg.) were suspended in 20 ml. of water, 10 mg. of manganese dioxide were added, and the whole boiled. 2N-Sulphuric acid was added dropwise until no more iodine was evolved. The iodine was collected in carbon tetrachloride and titrated against 0·01N-sodium thiosulphate.

Rhenium. This was estimated either spectrophotometrically by absorption of the α-furfuraldoxime complex measured at 532 μ [3] or as nitron per-rhenate after removal of iodide.

CHEMISTRY DEPARTMENT, IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, April 2nd,* 1958.]

[3] Meloche, Martin, and Webb, *Analyt. Chem.*, 1957, **29**, 527.